Original Communications

SEROUS ADENOFIBROMAS AND CYSTADENOFIBROMAS OF THE OVARY

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IN RECENT years we have encountered in our laboratory and have had sent to us from other clinics several examples of ovarian tumors which we have designated as serous adenofibromas and cystadenofibromas. The paucity of the English literature dealing with this type of tumor is impressive. Although rare, they constitute a definite subgroup of serous epithelial tumors of the ovary. In a review of the case reports of ovarian tumors in our files for the last twenty years, embracing a total of 26,000 gynecologic cases, 13 case reports of such tumors were discovered and collected, and one report was found in the general pathology files. Not all of these specimens came from our operating room, for many were sent here from other hospitals, some in Baltimore and some in other cities. It is interesting to note the various diagnoses under which these tumors are filed, particularly the older cases: fibromas, fibromas with inclusion cysts, cystic fibromas, serous cystadenomas or papillary serous cystadenomas, solid adenomas, etc.

The only report in the English literature of a tumor of this type is the case report of Wolfe[22] in 1927. The most complete report of the general subject is that of Oskar Frankl[6] in 1927. In this he describes seventeen cases of "fibroma ovarii adenocysticum." From the data

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available in Frankl's article and in the light of more recent knowledge, it seems that many of his seventeen cases are incorrectly classified. As Dworzak[2] and Meyer have pointed out he included in the group a number of Brenner type neoplasms which showed various degrees of the pseudomucinous cystic change seen in some Brenner tumors. At least four cases must be eliminated from his group. Certainly the cases reported in a later article (1934) by Oskar Frankl and Klaften[7] are examples of Brenner tumors. Neumann[14] reports two cases, one an adenofibroma and one a papillary cystadenofibroma, while the one reported by Fleischmann[5] in 1916 as "adenofibroma cysticum papillare ovarii" fits into this class except that the author describes solid cell nests. This again makes one suspect that the growth may also have been a Brenner tumor.

A review of the literature up to 1937 is found in the contribution by Robert Meyer in Henke and Lubarsch's *Handbuch der Speziellen Pathologischen Anatomie und Histologie*.[13] Even here there is insufficient data available in many of the cases cited, and absolute inclusion in this specific group is a matter of conjecture.

For example a case included by Spencer[18] in his report (1923) of ten ovariotomies in women over seventy years of age most certainly represents only cystic degeneration of an ovarian fibroma. Dworzak,[2] in 1932, reported a case which can unequivocally be considered a bilateral cystadenofibroma. Frankl's "fibroma ovarii adenocysticum" has been included as a special type of serous cystadenomas in Taylor's[20] recent suggested classification of ovarian tumors. This author suggested that the grossly solid Brenner variety with microscopic cysts having pseudomucinous lining be included as a special type under pseudomucinous cystadenomas. All in all, the literature on this type of ovarian neoplasm is extremely scant and much of it is questionable because of incomplete descriptions and more recent conceptions of various tumor types.

Wolfe described adenofibromas as "complex tumors of benign type in which epithelial and stromal elements simultaneously multiply." These tumors may grossly be quite minute (even microscopic) or very huge. The more solid type closely resembles the fibroma of the ovary or the solid Brenner tumor. The tumor is firm and compact, but minute cystic spaces may often be seen with the naked eye, while at times these cystic spaces may be relatively large. The intervening tissue is firm and white, with often a whorled arrangement of the strands of dense connective tissue. The cystic portions may enlarge, though rarely dilating in multilocular fashion, so as to occupy a large area of the tumor mass and to resemble the common serous cystadenomas. But, for inclusion in the group of cystadenofibromas at least a fourth of the total mass must remain solid, except perhaps for the presence of minute cysts. The more solid variety deserves the name of adenofibroma.

Interesting variations in size and position have been observed. The tumor in its early stage may appear as a tiny, dense, whitish area which stands out from the surrounding cortex, or it may produce only a minute raised area on the surface of a normal sized or slightly enlarged ovary. In other cases it may gravitate as an easily delineated nodule to a subcortical area and even to the hilus, or it may appear on the surface

as a small papilloma which on gross examination would be termed a papillomatous fibroma until stained sections revealed its adenomatous character. Even such small nodules may show marked dilatation of one or more of the cyst spaces, so that they are then more properly classed as small cystadenofibromas. In some instances the neoplasm may be multiple. In older literature one finds reports of much larger tumors than we encounter in our present, early-surgery period, and some of our own cases represent accidental findings at the operating table or in the pathology laboratory. The character of the fluid in the small and larger cyst spaces is usually thin and clear, serous in type, but in some cases it is thick and albuminous, and it may have a brownish tint.

Microscopically it is possible to establish a common denominator in the explanation of the various gradations of these tumors. As stated by Wolfe there are two constituent elements, the glandlike or cyst spaces and the fibromatous stroma. All of the small and large cyst spaces are lined by cuboidal or columnar, compactly placed, usually single-layered epithelium. The epithelium may be from two to four cells thick in areas, but this is uncommon and in many instances represents only tangentially cut portions. The nuclei are centrally or basally placed and are rather dark staining and elongated or circular. The cytoplasm is fairly uniform and moderately eosinophilic. Many and not uncommonly the majority of the epithelial cells have cilia. The adenomatous areas may be circular, elongated, or quite irregular. One often sees a papillary projection from the lining wall into the cyst spaces; these outgrowths have a dense fibrous core and are covered by the same type of epithelium as that lining the cysts. A papillary tendency was not usually seen on the surface of the tumor except in the case of the small cortical type, in which case the papillae were covered with germinal epithelium which frequently showed stratification. The so-called "psammoma-bodies" so often found in the serous cystadenomas are not uncommon in the adenofibromas and cystadenofibromas, particularly those of small size. They seem to develop as a result of calcification in the typical small glandlike space, and in one of our cases various transition stages, from early partial calcification of a cyst space and its lining epithelium to complete replacement, could be demonstrated. The stroma is exactly similar to the stroma of the common fibromas. There are compact bands and narrow strands of fibrous tissue running in all directions, often whorled, and much collagen can be found between the separate fibers. The connective tissue reaction is much more marked immediately about the cyst spaces, and in a few of the smaller tumors this pericystic reaction was the only evidence of fibromatous proliferation. With Van Gieson's stain all of this stromal tissue appeared to be connective tissue, but with the Masson's trichrome stain the fibers immediately about the cyst spaces took a peculiar red stain, like that of very young smooth muscle tissue.

Carcinomatous or sarcomatous changes would seem to be as possible in these tumors as in the serous cystadenomas or fibromas. The malignant change, when fully developed, so distorts the picture that it would be difficult to determine the nature of the benign precursor in many cases. None of our own tumors were malignant microscopically, and none of the patients later developed malignant changes in the contralateral ovary when it was conserved, in as far as we have been able to determine from the follow-up of the patients.

The gross picture and its variations, as well as the characteristic microscopic picture, will seem clearer when the case reports are studied and when the question of etiology is discussed. A short summary of the clinical and pathologic data in these fourteen cases is presented below. Unimportant and unnecessary detail has been eliminated as much as possible and in all cases when the typical lining epithelium is referred to this will mean the cuboidal or columnar, often ciliated type.

CASE 1.—(Gyn. Path. No. 29902.) This is a 52-year-old white female who complained of a crampy, aching abdominal pain for the previous six months. This pain was most marked in the left lower quadrant. Other facts in the history were of no importance and the menstrual history was normal. She was never married and never pregnant. The menopause was two and one-half years ago and she had had occasional hot flushes. On examination a tumor mass was found in the right adnexal region, and on Dec. 3, 1924, at Church Home Infirmary, Baltimore, Dr. T. S. Cullen removed the right ovarian tumor, the right tube, and the appendix. The other pelvic organs were noted as normal at operation. The specimen was sent to the Johns Hopkins Hospital laboratory and the ovarian tumor was found to be a bilobed, firm mass, the slightly larger lobe of which measured 4 by 2½ by 2 cm. On section both lobes were seen to be made up of firm, white, fibrous tissue in which there were numerous small, smooth-lined, glistening cavities. Microscopically the tumor showed dense fibrous tissue in whorls, most dense about the small cystic spaces lined by the typical epithelium. The largest cyst space measured 4 mm. in diameter.

Diagnosis.—Serous adenofibroma, ovary, right. Salpingitis, chronic, right. Normal appendix.

Nothing has been heard of the patient since the time of operation.

CASE 2.—(Gyn. Path. No. 38202.) This was an 87-year-old white female who complained of vague abdominal discomfort for the past one and one-half years. She was married but had never been pregnant, and the menopause was uneventful forty years previously. There was never any abnormal vaginal bleeding. Upon examination by her family physician, an abdominal tumor was found extending to the umbilicus. On April 28, 1932, at St. Agnes Hospital, Baltimore, Dr. Emil Novak did a total abdominal hysterectomy and a bilateral salpingo-oophorectomy. The specimen was sent to the Johns Hopkins Hospital pathology laboratory. The right ovary was replaced by a huge cystic tumor, 18 cm. in diameter, whose wall was thin except for about one-third of the total mass which was solid and quite firm. The cyst was filled with clear, straw-colored fluid, although there were some smaller locules filled with

old blood. Many of the locules presented minute papillary projections on the inner surface. The left ovary showed two small cysts filled with clear, straw-colored fluid. On microscopic section, these were found to be typical small serous cysts. The right ovarian tumor showed the same type of cyst wall with cuboidal to low columnar, often ciliated, epithelium, and at areas there were papillary projections into the cysts. The solid portion was densely fibrous with numerous small cysts lined with the same type of epithelium; a few of these smaller cysts also had papillary growths from the wall.

Diagnosis.—Papillary serous cystadenofibroma, ovary, right. Serous cysts, ovary, left. Atrophic cervix with Nabothian cysts. Endometrial polyp. Atrophic endometrium, myometrium, and tubes.

The patient has not been seen since operation and no information can be secured as to her status.

Case 3.—(Gyn. Path. No. 38437.) This was a 60-year-old white female who was first seen with difficulty in breathing and with vomiting for several hours prior to admission to the hospital. There had been considerable epigastric pain and on examination the abdomen was diffusely tender. A mass of an uncertain character was felt in the pelvis. No data were obtained of the previous health or the menstrual history. On June 17, 1932, at St. Agnes Hospital, Baltimore, Dr. Oliver did a bilateral oophorectomy, myomectomy (three small subserous nodules), and a cholecystectomy. A large calculus was found in the gall bladder. The ovarian tumors were sent to the Johns Hopkins Hospital Gynecologic Pathology laboratory, and they were both found to be about 6 cm. in diameter and fairly globular in outline. One tumor was solid and of a firm, fibrous nature on section. The other tumor was thick walled (about 1½ cm.), and in this wall minute cystic spaces were seen. There was a large cyst, occupying the central portion of the tumor and this was filled with clear, mucinous material. There were a few papillary projections on the wall of the cyst. On microscopic examination the solid tumor was found to be a typical fibroma, and the opposite one had a cyst lining of the typical epithelium; distributed throughout the firm fibrous wall were numerous small glandlike spaces lined by the same epithelium.

Diagnosis.—Papillary serous cystadenofibroma, ovary, one side. Fibroma, ovary, other side. Myomata uteri, subserous. Cholelithiasis and chronic cholecystitis. This patient cannot be traced.

Case 4.—(Gyn. Path. No. 44921.) This was a white woman, 60 years of age, who complained of vaginal bleeding of two years' duration, more intense in the past three weeks. The menses were regular and the menopause occurred eight years previously. There had been four pregnancies, and one of these resulted in an early miscarriage. The youngest child was thirty years of age. On examination bilateral adnexal masses were felt. On Dec. 2, 1936, Dr. Harry M. Nelson at the Womans Hospital, Detroit, Michigan, did a hysterectomy and a bilateral salpingo-oophorectomy. Dr. D. C. Beaver, director of the laboratory at this Hospital, sent Dr. Novak slides and photographs of these tumors. The photographs are self-explanatory for gross description (Figs. 1 and 2); the left, solid tumor measured 4.5 by 4 by 3 cm. and the right, partially cystic one, measured 5 by 4 by 4.5 cm. Microscopically there was the fibrous tissue overgrowth with many small cystic spaces lined by the

typical epithelium. The large cyst had the same type of lining epithelium, and on both sides papillary projections from the wall of the cyst spaces were seen. Psammoma bodies were seen on both sides.

Diagnosis.—Papillary serous adenofibroma, ovary, left. Papillary serous cystadenofibroma, ovary, right. Atrophic endometrium and endometrial polyps (which probably accounted for the postmenopausal bleeding).

This patient at present is alive and well, according to correspondence from Drs. Beaver and Nelson.
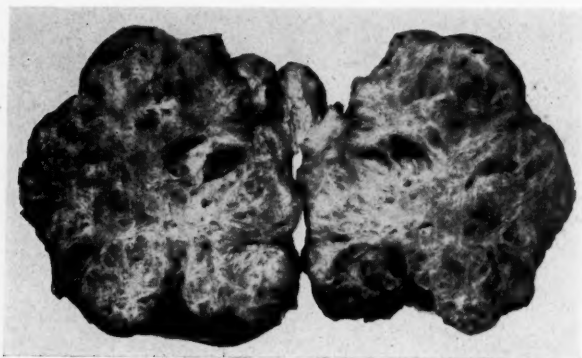

Fig. 1.—Case 4. Gross picture of the serous adenofibroma which replaced the left ovary. Psammoma bodies and minute papillary projections into many of the tiny cyst spaces were seen microscopically. About actual size. See Fig. 2 for tumor of the opposite ovary.

Fig. 2.—Case 4. Gross picture of the serous cystadenofibroma which replaced the right ovary. Psammoma bodies and a papillary tendency were seen on this side as in Fig. 1. A small accumulation of papillary projections can be seen here at the upper border of the largest cyst. About actual size.

CASE 5.—(Gyn. Path. No. 45368.) A 42-year-old colored female complained of pain in both lower quadrants for five weeks, prolonged menses, and continuous vaginal bleeding for the previous month. She had been admitted to the Hospital three months prior with a diagnosis of subacute salpingitis and pelvic peritonitis. Sulfanilamide therapy was given at this time with apparent good results. She had had two previ-

ous pregnancies and full-term deliveries; the youngest child was twenty-three years old. Bilateral tender adnexal masses were felt, and on July 28, 1937, Dr. Laman Gray did a subtotal abdominal hysterectomy and bilateral salpingo-oophorectomy. The right ovary showed a papillomatous, firm projection from the surface, about 1 cm. in greatest diameter. On microscopic section this was found to consist of dense fibrous tissue with a few very small, glandlike spaces lined by columnar or cuboidal epithelium.

Diagnosis.—Surface serous papillomatous adenofibroma, ovary, right. Endometrium, interval, non-secretory. Myomata uteri, intramural and subserous. Pyosalpinx, bilateral. Abscess, ovary, bilateral.

She was seen two and one-half years later, and although she had numerous complaints, examination, including pelvic, was without significant findings.

CASE 6.—(Gyn. Path. No. 46139.) A 58-year-old colored female was admitted with the complaint of left lower quadrant pain at intervals over the previous three years. Menses were always regular, and the menopause was uneventful eight years previously. She had three pregnancies: one a miscarriage, one a stillborn, and one a full-term delivery in which the infant died at the age of six months. Nodular pelvic masses were felt, and on Jan. 26, 1938, Dr. T. S. Cullen did a bilateral salpingo-oophorocystectomy. The right cyst was 10 cm. in diameter and the left was 3.5 cm. in greatest diameter. The cysts were multilocular and filled with clear, straw-colored fluid. In each there were dense solid portions which made up about one-half of the tumor mass. The fibromatous reaction and the small gland spaces with the typical lining epithelium were again seen in the solid portions on stained sections. The larger cysts were also lined with this epithelium.

Diagnosis.—Serous cystadenofibromas, ovary, bilateral. Atrophic tube, bilateral.

This patient was well except for occasional hot flushes two and one-half years after operation.

CASE 7.—(Gyn. Path. No. 48600.) This was a 31-year-old colored female who complained of pain in both lower quadrants of the abdomen for the previous nine months, and this pain had become constant in the left lower quadrant for the past three weeks. Over the previous year she had noted increasing enlargement of the abdomen. Menses were always regular and she had had two pregnancies, both of which ended in miscarriages one and two years previously. On examination a large cystic mass was found arising from the right adnexal area and extending to just above the umbilicus. On May 31, 1939, Dr. Henry Bennett did a right salpingo-oophorocystectomy. The cyst was found to be twisted slightly and adherent. On examination the mass was found to consist of two large cysts, and measuring 15 by 16 by 11 cm. and 16 by 20 by 9 cm., respectively. These were filled with thick, dark brown, gelatinous material, and there were several daughter cysts in the wall. Several small papillary projections were seen protruding into one of the cysts. The wall was 1 to 4 mm. thick, except at one border where there was a dense, firm, solid mass 5.5 cm. in its greatest diameter. The ovary was distinctly outlined and separate, except that the solid mass described was attached to one pole. The ovary measured 3 by 5 by 1.5 cm., and it contained a few small follicle cysts on section. The

solid part of the neoplastic mass revealed the characteristic fibrous stroma with small cystic spaces lined by the typical epithelium. The cyst walls all had the same type of lining and there were numerous small and moderate-sized papillary projections from the wall into the cysts. Psammoma bodies were frequent.

Diagnosis.—Papillary serous cystadenofibroma (papillomatous in type), ovary, right. Perisalpingitis, chronic, right. This patient was seen again two years after discharge and pelvic examination revealed the uterus to be adherent to the left, and there were no palpable adnexal masses.

CASE 8.—(Gyn. Path. No. 50470.) This was a 69-year-old white female who ceased menstruating at fifty-two years of age for a period of six months and then began to have apparently normal menses every three to six months. In September, 1939, she began to bleed continuously and a curettage at that time revealed adenocarcinoma of the fundus uteri. A full course of radium therapy was given. She had had six pregnancies and full-term deliveries; the youngest child was thirty-five years old. The menses were not unusual before the onset of the present illness. On examination at Johns Hopkins Hospital the uterus was found to be about three times normal size, and a partially cystic mass, about 7 cm. in diameter, was felt in the right adnexal area. On May 14, 1940, Dr. Richard TeLinde did a total abdominal hysterectomy and a bilateral salpingo-oophorectomy. The right ovarian tumor measured 8 by 4 by 3 cm. and one-half of this tumor was solid, the other half being cystic. The cystic part was filled with thin, clear fluid, and there were a few papillary processes in the cyst wall. Microscopically the section showed the fibromatous overgrowth with the small cystic spaces and the usual epithelial lining of both the small spaces and the larger cysts. Papillary projections were prominent and a few of the fibrous areas showed a moderate amount of hyaline degeneration.

Diagnosis.—Papillary serous cystadenofibroma, ovary, right. Cervicitis, chronic. Adenocarcinoma, fundus, uteri. Myomata uteri, subserous. Atrophic tube, bilateral. Atrophic ovary, left.

All efforts to contact this patient since discharge have failed.

CASE 9.—(Gyn. Path. No. 51214.) This was a 55-year-old white female whose chief complaint was pressure in the rectum. She had had a uterine suspension, appendectomy, and right oophorectomy ten years previously. Menses were normal, and the menopause occurred eight years prior to admission. This patient was operated upon in Binghamton, New York, by Dr. Francis O'Neill, and a description of the gross tumor and sections were sent to Dr. Novak at this Laboratory by Dr. Victor W. Bergstrom, Director of the Kilmer Pathological Laboratory, Binghamton, on Sept. 1, 1940. The tumor measured 11 by 8 by 4 cm., and it was somewhat nodular. On section there was a thin fibrous capsule and the tissue was yellowish, dense, fibrous, and often arranged in whorls. Stained sections showed the small glandlike areas in a dense fibrous field. The epithelial lining of these spaces was of the typical type.

Diagnosis.—Serous adenofibroma, ovary, left.

The patient is now living and well.

CASE 10.—(Gyn. Path. No. 51446.)   This was a 46-year-old white female who complained of vaginal bleeding of thirty-three days' duration.   Menses were always regular, and there were no data given as to her previous pregnancies, if any.   On examination the uterus was retroflexed and very nodular.   On Oct. 24, 1940, at Bon Secours Hospital,

Fig. 3.—Case 10.   Cross section of the left ovary, approximately actual size.   The two cortical adenofibromas, extending subcortically, are easily seen, and the cyst at the bottom was found to be a typical small serous cyst.
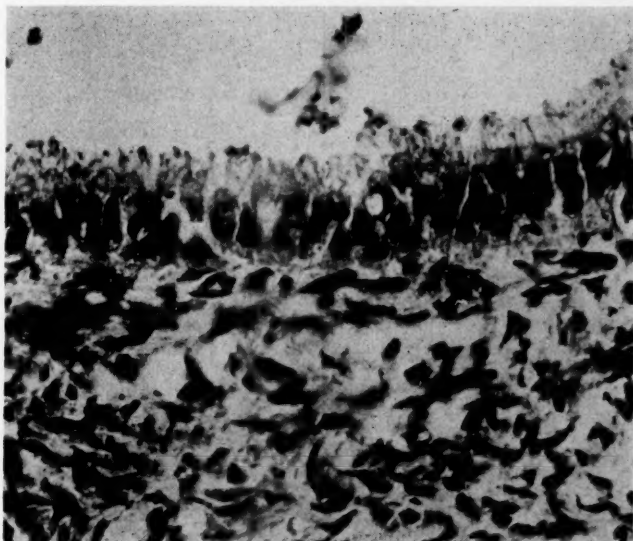

Fig. 4.—Case 10.   High power (×550) of the typical, single-layered, columnar epithelium lining the "glandlike" spaces.   Ciliated cells were more abundant here than in most of these neoplasms.

Baltimore, Dr. Emil Novak did a subtotal, abdominal hysterectomy and a right salpingo-oophorectomy.   The right ovary was slightly larger than normal and the surface was smooth.   On section two subcortical, solid nodules, were seen, the largest measuring 1.2 cm. in diameter.   At the operating table these were thought grossly to be

small Brenner tumors. Microscopically the solid areas contained small cystic spaces and one large cystic space (0.7 mm. in diameter), all of which were lined by this typical epithelium. The spaces were imbedded in a dense fibrous stroma.

Diagnosis.—Serous adenofibromas, ovary, right. Serous cyst, ovary, right. Endometrial hyperplasia. Myomata uteri, intramural. Normal tube, right.

This patient is alive and well one and one-half years postoperatively.

CASE 11.—(Gyn. Path. No. 51534.) This was a 40-year-old colored female who complained of pains off and on for twelve years in the left lower quadrant of the abdomen and of an abdominal tumor which she had felt for the past year. In this previous year she had backache and rather marked frequency of urination without burning. Menses were always regular, and there had been one pregnancy and full-term delivery nineteen years previously. On examination the uterus was replaced by a nodular mass extending to about midway between the symphysis and the umbilicus and filling the adnexal areas. On Nov. 22, 1940, Dr. Henry Bennett did a subtotal abdominal hysterectomy, salpingo-oophorectomy, right, salpingectomy, left, resection of small ovarian cyst, left, and appendectomy. The right ovary measured 3.5 by 2.5 by 1 cm. and the surface was wrinkled. On section a few small cysts were seen filled with clear, thin, fluid. Microscopically there was a central area 8 by 4 mm. which contained numerous small cysts of irregular shapes and without much fibrous reaction about them. In a microscopic area (1.5 mm.) just to the side of the cystic portion there was a denser portion in which were imbedded many small glandlike spaces. The fibrous tissue proliferation was more extensive here. The epithelial linings of all of these spaces and of the more cystic area described were of the typical type.

Diagnosis.—Serous adenofibroma, ovary, right. Endometritis, chronic. Myomata uteri, intramural, and subserous. Salpingitis, chronic, left. Salpingitis, isthmica nodosa, right. Endometrial cyst, ovary, left. Normal appendix. Postoperatively the patient developed an incisional infection and later a ventral hernia. On June 11, 1941, this hernia was repaired and pelvic examination revealed no enlargement of the remaining left ovary. She is now asymptomatic.

CASE 12.—(Gyn. Path. No. 52448.) This was a 29-year-old white female who complained of pain in the right lower abdomen for the past year. Menses were always regular. She had had three early spontaneous abortions in the previous five years, the last one being in April, 1940. Appendectomy was done at the age of thirteen. A small mass was felt in the region of the right ovary, and on April 30, 1941, Dr. Richard TeLinde did a right salpingo-oophorectomy. The right ovary was densely adherent to the adjacent structures. It measured 5 by 4 by 2 cm. The surface was covered with many fibrous tags, and there were about ten slightly elevated, small, firm areas. On section these firm areas were found to be minute cortical, dense, white structures. Microscopically these cortical areas showed heavy fibrous proliferation and numerous small cysts, all lined by the same type of epithelium seen lining germinal inclusion cysts. The areas were quite distinctly outlined and separate from each other. Many psammoma bodies were seen in all stages of formation.

Diagnosis.—Small serous adenofibromas, ovary, right. Follicle cysts and corpus luteum, ovary, right. Salpingitis, isthmica nodosa, right.

The patient is now well except for some persisting slight pain in the left lower quadrant.

CASE 13.—(Gyn. Path. No. 52750.) This was a 58-year-old white female who complained of brownish vaginal discharge which at times contained blood for the previous thirteen years. Thirteen years ago she had an ovarian cyst removed at another hospital, and no data were available, except that the patient said that it weighed thirty-one pounds. She never menstruated following this operation. Prior to the operation she had had two full-term, rather difficult, deliveries. A curettage was done by Dr. Leo Brady and the curettings showed adenocarcinoma of
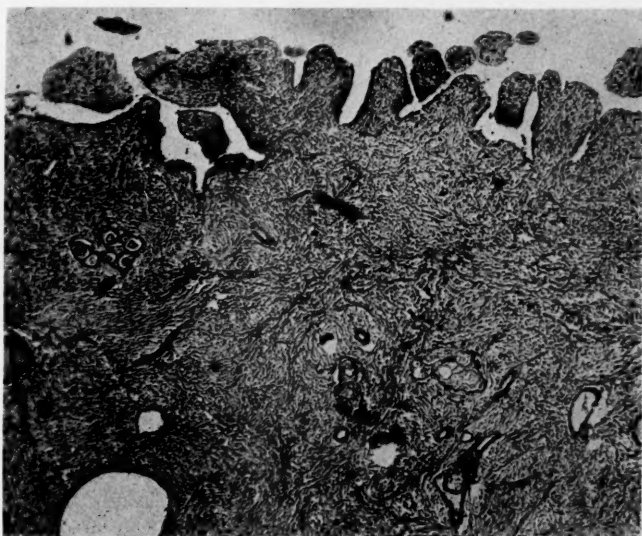

Fig. 5.—Case 12. Low power (×50) of a portion of one of the cortical adenofibromas in this case, showing the small "glandlike" spaces, the fibromatous proliferation, many psammoma bodies, and the surface papillary tendency.

the fundus uteri. Following 3,600 mg. hours of intrauterine radium and 6,000 r. units of deep x-ray therapy, Dr. Brady on June 16, 1941, did a total abdominal hysterectomy, right salpingo-oophorectomy, and appendectomy. The right ovary measured 3 by 2 by 1 cm., and projecting from one pole was a firm, white nodule which measured 1 cm. in diameter. On stained section the tissue of this nodule was dense and fibrous and scattered about were several small, irregular cysts which were lined by the usual epithelium.

Diagnosis.—Papillomatous serous adenofibroma, ovary, right. Atrophic cervix. Endometrium, postmenopausal, atrophic (no adenocarcinoma was found in numerous sections). Hypertrophy of uterus. Periuterine adhesions. Atrophic tube, right. Mucocele of appendix.

The patient was clinically well one month after discharge.

CASE 14.—(Gyn. Path. No. 17071.) This 50-year-old white female came to autopsy ten hours following removal of a chromophobe adenoma

of the pituitary which had produced progressive loss of vision over three years. She was quite obese, never pregnant, and menses were always regular. The menopause occurred five years prior to admission. At the age of twenty, there had been a pelvic operation of an unknown character. At autopsy the left tube and ovary were missing, and there were several moderate-sized intramural myomas. The ovary was about normal size, and projecting from one side was a thin-walled cyst about 4 cm. in diameter. The cyst contained clear serous fluid and the walls were smooth. On section numerous minute cysts were seen in the ovarian substance below this attached large cyst. Microscopically there was in this ovarian area and extending centrally a large collection of minute cysts imbedded in a dense fibrous stroma. These cysts were lined with
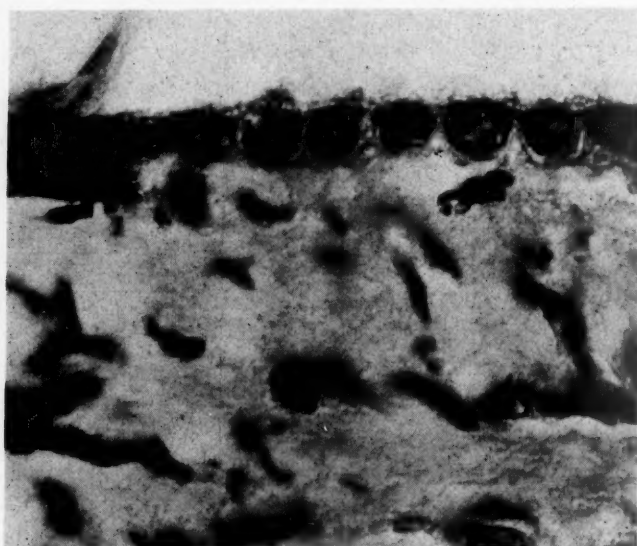

Fig. 6.—Surface germinal epithelium (×1200) of the ovary of a 46-year-old white female. This demonstrates the cilia which may rarely be found on uninvaginated surface epithelium. (Gyn. Path. No. 53139.)

the typical epithelium, as was the large cyst which seemed to arise from this area. The solid area with many cysts was about 1.5 cm. in diameter. At the border of this intraovarian lesion there was a minute circular fibroma without cystic contents. Psammoma bodies were seen.

Diagnosis.—Serous cystadenofibroma, ovary, right. Normal tube, right. Myomata uteri, intramural.

In summary, therefore, our series includes 8 adenofibromas and 8 cystadenofibromas. One adenofibroma was associated with a cystadenofibroma of the opposite side, and in one case there were bilateral cystadenofibromas. Two adenofibromas and one cystadenofibroma were of the surface papillomatous type, and in 2 cases there were multiple cortical or subcortical adenofibromas. The remaining tumors completely or almost completely replaced the ovary. Only one adenofibroma presented papillary projections into the small cyst spaces, while 5 of the cystadenofibromas grossly or microscopically revealed this variation.

All but 4 of these tumors were palpable preoperatively, either as tumor masses or as enlarged, atypical ovaries; 3 of them [a surface papillomatous adenofibroma (Case 5), adenofibromas (Case 10), and an adenofibroma (Case 11)] were incidental laboratory or operating room findings, and the fourth was found at autopsy. Had a pelvic examination been done in this autopsy case the associated cyst could undoubtedly have been palpated.

The co-existing uterine, tubal, and contralateral ovarian pathology was without any apparent significance. The opposite ovary in 2 cases presented the same type of tumor or a variant thereof, and in one case there was a large fibroma on the opposite side. In the other cases the opposite ovary was not removed at operation because of its normal character, or when removed it was normal or it revealed totally unrelated pathology (except for a serous cyst on the opposite side in one case and two serous cysts in the same ovary in another case). Myomas of the uterus were found in 6 cases. This may seem a high percentage, but in proportion to the incidence of myomas in our total operative cases, which include a large number of colored patients, it is not excessive. In many of these 14 cases the myoma was the sole or major contributing factor to operative intervention. Two of the 4 colored females in this series had myomas. Salpingitis and other pelvic inflammatory lesions were no more frequent than would be expected in any consecutive series in our Laboratory. The presence of adenocarcinoma of the corpus uteri in 2 cases is interesting, but of no great significance, except that it constituted the indication for operation in these patients.

In evaluating the symptoms, abdominal pain was the presenting complaint in nine of the cases. In one of the cases it was the pain of pelvic inflammatory disease and in another the pain of cholelithiasis. In one case pain was due to the pressure of large myomas. In the remaining 6 cases the pain was directly related to the ovarian neoplasm or neoplasms. In only 2 cases had the patient noted the tumor growth prior to operation.

Five patients complained of abnormal uterine bleeding. Superficially this might suggest that such tumors may exhibit endocrine properties, but in all of these cases the other existing pathology more adequately explained the bleeding:

Case 4: Endometrial polyps
Case 5: Myomata uteri, intramural and subserous; pyosalpinx, bilateral; abscess, ovary, bilateral
Case 8: Adenocarcinoma, fundus uteri
Case 10: Endometrial hyperplasia; myomata uteri, intramural and subserous
Case 13: Adenocarcinoma, fundus uteri

In 11 of Frankl's cases there were urinary complaints, but in only one of my series was this noted, and in this case it was probably due to

pressure from myomas. This discrepancy in figures is probably explained by the great size of the tumors in Frankl's group.

Here, as in all other reported cases, the age incidence is found to be very characteristic.

TABLE I. AGE AND DISTRIBUTION OF CASES

AGE	FRANKL'S TYPICAL CASES	WOLFE	NEUMANN	DWORZAK	PRESENT	TOTAL
20-29					1	1
30-39					1	1
40-49	4	1	1		3	9
50-59	6				5	11
60-69	2		1	1	3	7
70-79	1					1
80-89					1	1
Totals	13	1	2	1	14	31

Other reported cases in which the pathologic diagnosis seems doubtful are not included in Table I. In these 31 cases, all but 2 are forty years of age or over (93.5 per cent) and all but 11 are fifty years of age or over (64.5 per cent). It is well known that with increasing age and ovarian atrophy, fibromatous reaction and replacement becomes more common, and with the corrugation of the surface and the invagination of the germinal epithelium, germinal inclusion cysts are a frequent finding. It is not surprising, therefore, that these tumors, the chief pathologic feature of which consists of fibrous tissue proliferation about numerous small "inclusion-like" cysts, should be more common beyond the fourth decade of life and particularly after the menopause.

Two patients of this group were one to five years postmenopausal, 3 were five to ten years, 2 were ten to twenty years, and 1 forty years. There were no accurate menstrual data on one patient, aged 60 years, who was obviously past the menopause. Dworzak felt that the early menarche and early menopause in his patient and in many of Frankl's patients were significant. Early menopause means early ovarian inactivity, and only in this way would it seem to play a part. A survey of these cases as to menarche, parity, and age of menopause shows no significant relationship.

The follow-up in many of these cases is not as adequate as one would desire. In those cases which we have been able to follow, there is no evidence that a similar tumor has developed in the remaining ovary, nor is there any evidence that these tumors were in any sense malignant. Microscopically there was no suggestion of malignancy, and the only alteration in the usual epithelial character was a slight piling up of the lining cells in some cases. Any one familiar with the microscopic picture of benign serous cystadenomas realizes that this is a frequent finding. As previously stated, it is conceivable that carcinoma might develop from the epithelial elements or sarcoma from the connective tissue.

We have not had an opportunity to trace such a transition, and were malignancy to occur, the gross and microscopic picture would probably be so altered that it would be impossible to say that the tumor might have originally been an adenofibroma or cystadenofibroma.

ETIOLOGY

Since the work of Robert Meyer[12] in 1916, practically all gynecologists are agreed that serous cysts and serous cystadenomas are derived from the germinal epithelium. Meyer felt that all ciliated epithelial tumors were derived from the germinal epithelium. Goodall,[10] in 1920, demonstrated that the Wolffian tubules unite outside the ovarian structure in embryonic life and that the medullary rays and rete ovarii are derived directly from the germinal epithelium. Therefore, if serous tumors are derived from remnants of these structures in the adult ovary, they are indirectly of germinal epithelial origin. As Goodall states, there is no tissue in the human body which can equal the metaplastic power of this epithelium. Ciliated epithelial cells have been found on the surface of the ovary by Pfannenstiel,[16] Flaischlein,[3] Walthard,[21] de Sinéty et Malassez,[17] Goodall,[10] and others. In several cases with corrugations of the surface and invaginations of the surface epithelium, the author has found ciliated epithelium, both in the sulci and over the gyri, although never as marked as in the germinal inclusion cysts.

The similarity of the epithelial lining of the cyst areas in the adenofibromas and cystadenofibromas to that of the invaginating surface epithelium and the germinal inclusion cysts places this group in the serous epithelial class. This agrees with the etiologic impression held by Dworzak and Wolfe. Wolfe feels that the beginning is a fibromatous surface sprouting from the ovarian cortex which is later invaded by the somewhat piled-up germinal epithelium. This burrows in narrow, zigzag, elongated channels into the depths of the fibromatous stroma. The fact that the cyst spaces in the adenofibromas are comparatively regular in outline and the finding of small cortical and slightly larger central tumors would lead one to expect that the invagination preceded the fibromatous reaction and that the tumor then progressed centrally or peripherally. The cyst spaces probably multiply by budding and progressive invagination. We have called the surface fibromas, which show the long, twisting narrow epithelial channels in a dense connective tissue matrix, intracanalicular fibroadenomas, because of their striking resemblance to the well-known intracanalicular fibroadenomas of the breast. In the past twenty years in our laboratory, we have had 9 of these tumors, all less than 3 cm. in diameter and none as large as cited by Taylor.[19] In our cases, we have not included those which were an integral part of an associated cyst and projected into it from the cyst wall. These were preponderantly in elderly females, and psammoma bodies were even more frequent than in the adenofibromas and cyst-
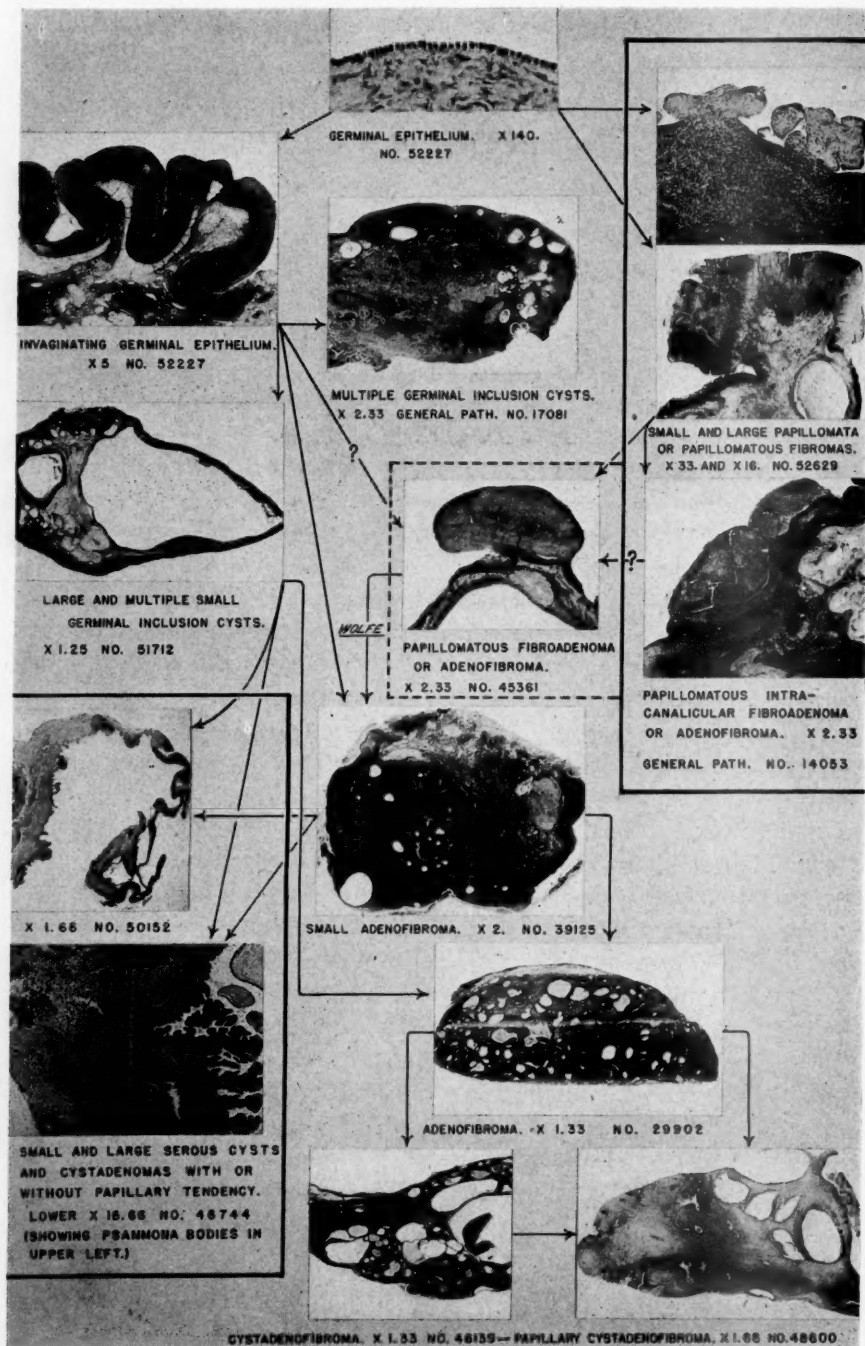
Fig. 7.—Photomicrographic diagram of the probable development of serous adeno-fibromas and cystadenofibromas from the germinal epithelium and the relationship to serous cysts and cystadenomas and papillomatous fibromas. For discussion see body of the paper under etiology.

adenofibromas. Microscopically one feels that these epithelial channels in the intracanalicular fibroadenomas are still connected with the surface.

Fig. 7 represents what most logically is the etiology of the adeno-fibromas and cystadenofibromas of the ovary. Our files have been searched for a typical example of each step in this process, and an effort has been made with these photomicrographs to be as graphic and understandable as possible. The tissues from which these tumors are derived are the germinal epithelium with its cuboidal and occasional peg-shaped, and often small round basal ("germinal"?) cells, and the underlying tunica albuginea, and fibrous cortical stroma. Some un-known factor can stimulate activity in these tissues in either of two possible directions. The fibrous stroma may begin to grow and produce the common papillomatous fibroma. The stromal proliferation in turn activates the overlying epithelium, and it is often seen to pile up, and it may penetrate the fibroma in narrow tortuous channels and form the intracanalicular fibroadenoma. On the other hand the epithelial chan-nels, as Wolfe believes, may partially or completely be nipped off to pro-duce a papillomatous adenofibroma or fibroadenoma. It is then possible for this to grow and become the large adenofibroma or cystadenofibroma. If this last step were the usual process, the ovary on this side would be expected to remain relatively distinct and attached at one pole, but this was not so in most of the large tumors of this series. More fre-quently the germinal epithelium invaginates from the ovarian surface, is pinched off, and produces germinal inclusion cysts. Gardner[8] states that these are seen most commonly in the presence of pelvic inflamma-tion and subsequent adhesions, but atrophic and atrophying ovaries of the female past forty years of age have been the site of predilection in our experience, as stated by Novak.[15] As the epithelium dips into the surface sulci, it can often be seen to pile up slightly and to assume a more compact cuboidal or columnar character, and it is often ciliated; at times this epithelium resembles tubal and more rarely endometrial epithelium. The inward sprout of germinal epithelium is then com-pressed in its proximal portion, leaving a typical inclusion cyst. By budding of this sprout and by a similar process elsewhere, multiple cortical inclusion cysts are formed, or in other cases a distinct cortical or subcortical nodule of many small cysts and marked pericystic fibrous tissue proliferation. The isolated or widely distributed germinal in-clusion cysts usually show little or no fibrous overgrowth about them. The single, large inclusion cyst or the definite nodule may enlarge pri-marily into a single or multiple cystic structure, constituting the well-known serous cyst or serous cystadenoma, with or without papillary tendency. The small adenofibroma may show neoplastic growth and may completely replace the ovary to form the large adenofibroma or, because of enlargement of some of the cyst cavities it gives rise to the cystadenofibroma, with or without papillary tendencies.

CLASSIFICATION

It seems that these tumors etiologically must be considered a special group under the serous epithelial tumors or, as Taylor has classified them, a special type of epithelial tumor under the heading of serous cystadenoma. It is not my wish further to complicate the already complicated classification of ovarian tumors, but these tumors comprise a definite group. The name of serous cystadenoma alone does not adequately describe tumors which include a solid, fibrous portion with the numerous, minute, "glandlike" spaces characterizing the cystadenofibromas. Certainly it is not adequate for the grossly solid or minutely cystic adenofibroma. If one-fourth or more of the total space occupied by the cystadenoma type of tumor is solid (in a fibroma-like manner), then it should be called a cystadenofibroma. The prefix of serous to these tumors is indicative of their etiology. Because of the possibility of malignant change, the epithelial elements must receive first consideration, and to classify the neoplasm as a mere variant of the fibromas would be unwise.

SUMMARY

1. Fourteen cases of serous adenofibromas and cystadenofibromas of the ovary are reported. These tumors correspond to the typical "fibroma ovarii adenocysticum" of Frankl, and Wolfe's case in 1927 is the only one previously reported in the English literature.

2. The tumors were found to be made up of two component parts, a dense connective tissue matrix in which were imbedded numerous small cystic spaces lined by compact, single-layered, cuboidal or low columnar, often ciliated epithelium. "Psammoma-bodies" and papillary tendencies were frequent.

3. Grossly the tumors were firm and solid, with minute cystic spaces (adenofibromas) or partially cystic with at least one-fourth of the mass solid (cystadenofibromas).

4. In two cases the neoplasm was bilateral, and in 3 cases the neoplasm was an incidental laboratory finding.

5. There was no constant associated pelvic pathology of significance, although myomata uteri were found in 6 cases.

6. Pain was the most common presenting complaint in nine instances, and in 6 of these cases it could be definitely related to pressure of the tumor.

7. No endocrinologic importance could be attached to these tumors. Five cases of abnormal vaginal bleeding were adequately explained by associated pelvic pathologic conditions.

8. The most striking clinical feature was the age of the patients. In a total of 31 tumors of this distinct group collected from the literature and including this series 29 (93.5 per cent) were forty years of age or over and 20 (64.5 per cent) were fifty years of age or over.

9. Malignancy (clinically or microscopically) was not observed in any of these cases, in spite of the fact that the potentialities in this respect would appear to be as great as in the serous cystadenomas and the fibromas.

10. A chart and discussion portraying the concept that these tumors are of germinal epithelial origin and emphasizing their close relationship to serous cystadenomas and papillomatous fibromas is shown.

11. It is suggested that these tumors be classified as a special type of epithelial tumor of the ovary under the subhead of serous cystadenomas, as previously suggested by Taylor.

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SEVERE POLYNEURITIS DUE TO VITAMIN B DEFICIENCY IN PREGNANCY

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IN 1932 the author reported five cases of severe polyneuritis following pernicious vomiting of pregnancy under the title of "Toxic Neuronitis Complicating Pregnancy."[8] Since that time fifteen additional cases have been observed. In those intervening years from 1932 to 1941 further studies by many investigators have proved that the condition is due to a vitamin B deficiency and can no longer be ascribed to a "toxemia developing during pregnancy."

Beriberi has long been known in the Orient and has been reported as a complication of pregnancy. In some instances the symptoms have been mild[9] and in some others so severe as to result in death. Theobold[14] suggested in 1930 that the neuritis of pregnancy was due to a vitamin B deficiency, because the neuritic form of beriberi in Bangkok was much higher in the pregnant woman than in the nonpregnant woman, and because the symptoms of beriberi are indistinguishable from the polyneuritis of pregnancy. Some authors,[2, 5, 7, 10, 18] however, believe that the lack of only vitamin B_1 will not cause the nervous lesions of degeneration and suggest that a deficiency of vitamin A or of other factors of the vitamin B complex is also necessary.

The deficiency of vitamin B_1 may arise from numerous factors: inadequate intake, inadequate absorption, or increased utilization, such as occurs in prolonged illness, in acute febrile conditions, or in pregnancy.

Many diets are inadequate as to vitamin B_1 content. Various investigators[1, 4] state that in the nonpregnant individual the diet should contain 150 to 250 units per day.

The onset of a pregnancy increases the requirement of vitamin B_1, and most authors state that the intake should be doubled during pregnancy and again increased during lactation.[4, 13, 17]

Williams, Griffith, and Fralin[17] studied the vitamin B_1 intake in the diet of 91 pregnant women, using approximately 500 units as the adequate intake level per day. On this basis only 37.17 per cent of their patients had an adequate intake.

Horwitz and Farley[6] studied 100 women estimating the O.B.T. principle in the urine and reported on 86 cases. Thirteen women had a low level; hence 15 per cent had a low intake of vitamin B.

Stahler[12] estimated the amount of vitamin excreted in the urine after daily administration of 10 mg. of thiamin intramuscularly for four days. Of the 40 mg. given, the normal nonpregnant woman excreted 46 per cent, the normal pregnant woman 30 per cent, and the polyneuritic woman 11 per cent. The polyneuritic pregnant woman retained more of the vitamin because there was a lack of it in the tissues.

The severe cases of polyneuritis with which this paper is primarily concerned develop early in pregnancy, and are usually preceded by a severe pernicious vomiting of pregnancy. Some cases have been reported in which vomiting did not occur. The deficiency of vitamin B_1 in pernicious vomiting is brought about first by a lack of food intake, second by a failure of retention of food ingested, and third by a high carbohydrate diet accompanied by administration of large amounts of intravenous glucose.

The usual history is one of vomiting with attempts at high carbohydrate ingestion and the administration of glucose, with or without improvement of the patient and the onset of a peripheral neuritis. The first symptoms are those of generalized weakness, pain in the calves of the lower legs, numbness, and tingling of the hands and feet, and inability to walk. Careful examination at this time reveals atrophy of muscles and overlying skin, and diminished or absent reflexes in the envolved areas. The weakness and paralysis ascends the body. Retention of urine or incontinence with overflow, constipation, paralysis of the abdominal muscles, paralysis of the accessory muscles of the chest, and involvement of the bulbar area with diaphragmatic paralysis, tachycardia, difficulty with phonation and deglutition occur in order. Mental confusion of the Korsakoff type is frequently present.

Case 1.—(No. 32497, University Hospital.) The patient, aged 26 years, was admitted July 24, 1930, to the Neurological Service. Patient had a regular menses July 1, 1929, and about Sept. 1, 1929, began to have nausea and vomiting for which she was treated. She improved slightly but was required to stay in bed. About December 1 she began to have severe pains in the legs with numbness and tingling. Because of continuation of the nausea, vomiting, and leg pains, a therapeutic abortion was performed on Dec. 27, 1929. The patient was unable to get out of bed until March, 1930. On admission she was wearing braces on both feet and required crutches for walking or standing.

The general physical examination was essentially negative except for the local findings of the lower extremities. This revealed a bilateral foot drop, tenderness over both achilles tendons, deep pressure pain over the calf muscles, and reversal and adduction of knees.

Patient was given massage and electrical stimulation and was dismissed Aug. 18, 1930, at her own request. There has been no known follow-up.

Case 2.—(Methodist Hospital, service of Dr. W. H. Taylor.) Mrs. M. C., white, married, aged 27 years, para ii, gravida iii. The last regu-

lar period began May 15, 1926. At the fifth month there was nausea and vomiting. After two months of vomiting, there developed muscular weakness, areas of anesthesia of the extremities, and cramps in the legs, and signs of a pre-eclampsia, Grade II. Because of failure of conservative therapy and disappearance of fetal heart tones, a medical induction was done. The patient died twenty-four hours after delivery, the death being due to polyneuritis rather than the toxemia. No vitamin therapy was given.

CASE 3.—(Methodist Hospital, service of Dr. W. H. Taylor.) Mrs. L. H., white, married, aged 36 years, para i, gravida iii. The last regular period began Jan. 4, 1933. Nausea and vomiting began Feb. 23, 1933, and persisted in spite of dietary regulations and sedation. On April 24, 1933, she developed pain along the left supraorbital nerve, and in eight days there was ptosis of both eyelids, bilateral facial paralysis, weakness of extremities, muscular cramps, paralysis of the diaphragm, evidence of bulbar paralysis, mental confusion, and retrobulbar optic neuritis. She was given vitamin B therapy, but because of failure of therapy a vaginal hysterotomy was done. For a few days there was no change in the patient's condition, then there was slow improvement with eventual recovery in six months. (Criticism: Vitamin therapy of forty-eight hours' duration was insufficient and not a fair trial.)

CASE 4.—(No. 45620, Immanuel Hospital.) Patient, white, aged 22 years, gravida i, last period Jan. 7, 1933, developed nausea and vomiting about the middle of February, which became severe about April 12. She was treated conservatively with sedation and intravenous glucose, and improved considerably but noted some tingling of the fingers. After one week there was a recurrence of vomiting and the development of a polyneuritis which followed a rapidly progressive course of the ascending type. She died four hours after a vaginal hysterotomy. No vitamin B therapy was given.

CASE 5.—(No. 47937, University Hospital.) Patient, white, married, aged 24 years, primigravida, last period in March, 1934, had marked nausea and vomiting with the development of a typical vitamin B deficiency including polyneuritis. She aborted spontaneously Aug. 15, 1934, and was seen by the author four days later. On admission there were the typical signs of vitamin B deficiency, including polyneuritis and a Korsakoff psychosis. She received intravenous fluids as well as brewers' yeast and liver extract intramuscularly. She slowly improved, being dismissed from the hospital thirty days after her admission and was completely recovered one year later.

CASE 6.—(Methodist Hospital, service of Dr. W. H. Taylor.) Mrs. P., married, white, aged 24 years, primigravida. Her last period occurred Aug. 9, 1934. This was followed by some nausea and vomiting for two months. At the fourth month she developed a left supraorbital neuritis, paralysis of the left facial nerve and a general polyneuritis. Under treatment with vitamin B, liver extract and iron she gradually improved. She was delivered by cesarean section at term because of cephalopelvic dysproportion. The baby weighed seven and three-fourths pounds. The patient made a complete recovery.

CASE 7.—(No. 53038, Immanuel Hospital.) Mrs. A., married, gravida i, white, aged 20 years, was admitted May 17, 1935. The patient had her last normal period on May 1, 1935. She had some nausea and vomiting which was mild at first and then became severe about May 1.

On hospitalization she was found to be slightly dehydrated. She was treated with intravenous glucose and rectal feedings, and after temporary improvement, she had a resumption of vomiting associated with a pulse rate of 100 to 110, hyperactive reflexes, tenderness in extensor muscles of the lower legs, and numbness and tingling in hands and feet.

She was seen in consultation and, because of the above findings, a therapeutic abortion was done May 25, 1935. She made an uneventful recovery and was dismissed on May 31, 1935, receiving four brewers' yeast tablets daily, and a high vitamin diet.

She had a normal period Nov. 25, 1936. She was seen on Jan. 14, 1937, and a diagnosis of pregnancy was made. She was given brewers' yeast tablets, three daily, and had only one or two attacks of nausea. She was delivered on Sept. 5, 1937, of a normal female child weighing 8 pounds.

CASE 8.—(No. 54244, University Hospital.) Patient, para 0, gravida i, aged 22 years, was admitted July 24, 1936. Last normal period occurred in November, 1935. There was some nausea during early weeks of pregnancy, but severe vomiting began in February, 1936. She was admitted to a hospital, given "hypos and food by vein" and after eleven weeks was dismissed improved. After several weeks she relapsed and was admitted to another hospital and then transferred to the University Hospital. She had lost 65 pounds in weight, was mentally dull, and physically weak.

Neurologic examination showed generalized muscle weakness, all types of sensation essentially normal except at the very peripheral portions, and reflexes normal except for absent knee and ankle jerks, bilateral.

A mild secondary anemia was present. She was treated with vitamin B complex, iron, and a high vitamin diet.

The patient improved rapidly and was dismissed Aug. 25, 1936, but readmitted August 30, in labor, and after normal labor delivered a normal female child, weighing four pounds one ounce. The puerperium was normal and she was dismissed on Sept. 9, 1936, completely recovered.

CASE 9.—(No. 58999, University Hospital.) Patient, colored, para 0, gravida iii, aged 28 years, was admitted Nov. 29, 1937. Last menstrual period Aug. 6, 1937. She began to have vomiting about Sept. 30, 1937. At first vomiting mild, but rapidly became severe and she was admitted to a hospital where she was treated with hypos and intravenous fluids. She was dismissed from that hospital Nov. 19, 1937, at which time she was improved except for the onset of double vision. After her dismissal she continued to vomit, complained of general weakness, pain in the legs, and tenderness to touch in the legs. Three days before admission patient became mentally confused and passed into unconsciousness. For twenty-four hours before admission there was some vaginal bleeding.

Examination on admission showed a well-developed, dehydrated, colored female, in coma; all muscles were weak, flaccid, and all reflexes hyperactive. Patient was given a blood transfusion of 500 c.c., and 500

c.c. of 25 per cent dextrose solution. She failed rapidly and died twelve hours after admission.

Autopsy: Bronchopneumonia, pregnancy, acute degeneration of myelin sheaths of peripheral nerves.

CASE 10.—(No. 62853, University Hospital.) Patient aged 27 years, para iii, gravida iv, admitted Dec. 29, 1938. Last menses occurred in August, 1938. About Nov. 1, 1938, she began to have morning vomiting. Two weeks later she reported that she tired easily and wanted to sleep a great deal. From the middle of November until December 1, she vomited constantly. Although vomiting ceased, she had extreme anorexia and ate practically nothing. One week prior to admission she became irrational. Examination revealed a well-developed, well-nourished female, talking incoherently, skin very dry, pulse rate 160; there was tenderness over the muscles of the lower extremities to pressure; reflexes were normal except for absent knee and ankle jerks. Temperature was 102° F. She was given a high caloric, high vitamin diet, at first being fed by nasal catheter. This latter method was discontinued after one week when patient took food well. She was given thiamin chloride, 18 mg. daily, and nicotinic acid, 100 mg. daily. Her hemoglobin was 40 per cent, so she was given a transfusion of 500 c.c. of citrated blood. After two weeks molded plastic splints were placed to prevent foot drop and the dosage of thiamin chloride was increased to 80 mg. daily. In spite of this, mental confusion continued, and the patient complained of extreme pain in the lower extremities. By Feb. 1, 1939, the patient was clear mentally, but there was some foot drop. The dose of thiamin chloride was reduced to 15 mg. daily, the nicotinic acid to 40 mg. daily. Oleum percomorphum to 60 drops daily, and ferrous sulfate to 12 gr. daily were added.

Improvement was steady and slow, and the patient was dismissed on March 9, 1939. She was delivered at term of a normal child. Recovery was slow but complete one year after delivery.

CASE 11.—(No. 63941, University Hospital.) The patient, white, aged 30 years, was delivered September 17, 1938, of a premature child which survived. The puerperium was complicated by the development of a paralysis of the right serratus anterior muscle, thought to be due to a vitamin deficiency. Recovery was slow in spite of a diet reinforced with vitamin B.

Patient menstruated beginning Dec. 12, 1938. She had slight nausea but rapidly developed signs of a polyneuritis in a mild form. In spite of therapy (15 mg. thiamin chloride a day), the patient failed to improve and a vaginal hysterotomy was done May 9, 1939. Improvement began within a week, and complete recovery occurred in two months.

Criticism: Therapy was insufficient as to dosage and more B fractions were given.

CASE 12.—(No. 66277, University Hospital.) Patient, aged 26 years, gravida i, was admitted July 29, 1939. The last menses began April 26, 1939. Nausea and vomiting began the middle of May and increased in severity, and then decreased about July 1. She developed polyneuritis with blurring of vision and mental confusion. These findings and a secondary anemia were present on admission. She was given a

high vitamin diet, several blood transfusions, and 20 mg. of thiamin chloride daily with brewers' yeast. She gradually improved and was delivered Jan. 4, 1940, of a normal baby after a normal labor. Lactation was insufficient. Recovery was complete by June, 1940.

CASE 13.—(No. 67303, University Hospital.) Patient, aged 30 years, para ii, gravida iii, was admitted April 6, 1940. Patient's last menstrual period occurred on July 5, 1939. Vomiting began in August and continued until the latter part of December. In the early part of December she began to have soreness in her muscles, and on December 7 she became paralyzed in her lower extremities and had been confined to her bed since. She was seen by a physician in the latter part of December. He recognized the condition as one of polyneuritis. He treated the nausea, and placed her on a regime of a high vitamin diet with thiamin chloride, 10,000 units weekly. She made a slow convalescence and on admission to the hospital was in excellent physical condition. The only abnormal findings of note were wasting of the muscles of the legs, tenderness of the muscles of the calf of both legs, and inability to walk unassisted. Reflexes were diminished in the lower extremities.

Normal onset of labor occurred on April 8, 1940, resulting in a spontaneous delivery of a normal male child, weighing 7 pounds 10 ounces. Convalescence was normal.

Treatment during stay in hospital consisted of brewers' yeast tablets (Meads) 45 tablets daily; thiamin chloride, 15 mg. daily; oleum percomorphum drops, 40 daily.

CASE 14.—(No. 68191, University Hospital.) Patient, aged 31 years, para iii, gravida iv, entered the hospital July 6, 1940. She had been in reasonably good health until July 2 when, after some exertion, she collapsed and had to go to bed. On July 4 she began to have generalized aches and pains, some nausea and vomiting and on July 6 she noted dimness of vision.

During pregnancy the diet had consisted of pork meat, canned and dried fruits and vegetables but with little or no milk or fresh fruit or vegetables. On examination a typical polyneuritis was present as well as a secondary anemia. She was placed on a high vitamin diet, 132 mg. of thiamin chloride and 300 mg. of nicotinic acid daily. She recovered rapidly and was delivered of a normal child on Sept. 16, 1940.

CASE 15.—(No. 68376, University Hospital.) Patient, aged 28 years, para ii, gravida iv, entered the hospital April 25, 1940. The last menses began Oct. 26, 1939. The patient began to have nausea and vomiting shortly after her last period, and it became so severe that she was hospitalized from December 8 to 18, inclusive, during which time she was given the usual intravenous glucose-saline solutions and little or nothing by mouth. After her dismissal, she continued to have vomiting of a less severe type until March 1, 1940. About April 10 the patient noticed blurring of vision, edema of hands and feet, headaches, and numbness of extremities.

Examination revealed a well-developed, well-nourished female. The teeth were badly decayed. A few fissures appeared at the corners of the lips. A pregnancy of approximately six months' duration was

present.   The skin was dry and scaly over the elbows and the shins. There was some edema of the hands and the feet.

Hemoglobin was 75 per cent; basal metabolism, 7 per cent.   Urine showed nothing abnormal.

She was placed on a high vitamin, high caloric diet with addition of thiamin chloride, 10 mg. daily.   Brewers' yeast, 60 tablets daily, was given with thyroid, gr. ½ twice daily.

Neurologic examination was essentially normal.

She was dismissed greatly improved on May 10, 1940.   The patient was readmitted on July 24, 1940, with membranes ruptured but no pains.   After forty-eight hours, she was given castor oil and quinine induction.   Labor lasted two and one-half hours, and she was delivered of a normal male child.   The puerperium was normal and the patient was dismissed Aug. 5, 1940.

In the main the histories and physical findings follow the typical cases previously reported.   One notes, however, the frequency of ocular symptoms.   Three patients complained of blurring of vision, and in one patient there was retrobulbar optic neuritis.   This is an incidence of 26.6 per cent of ocular symptoms.   No previous reports have carried such a high incidence.

The reports of 130 cases (19 to 59) of severe polyneuritis in the literature were reviewed, and with the 15 cases herein reported, a total of 145 cases are available for study.   Some of the protocols are incomplete in all details and not all of the cases can be included.

One hundred and five patients received no vitamin B complex or vitamin B_1 therapy.   Forty patients were treated with varying amounts and varying fractions of the vitamin B complex.

In the total series there were 40 deaths, or a mortality of 27.5 per cent.   Thirty-seven of the deaths occurred in the 105 patients receiving no vitamin B complex therapy, an incidence of 35.2 per cent, while only 3 of the 40 patients receiving vitamin B complex therapy died, an incidence of 7.5 per cent.

The termination of pregnancy in 131 cases was studied[19-59] and recorded in Table I.

TABLE I

TYPE OF DELIVERY	TOTAL SERIES			NO VITAMIN THERAPY			VITAMIN THERAPY		
	NO.	DIED	%	NO.	DIED	%	NO.	DIED	%
Abortion, induced	62	19	28.3	53	17	32.0	9	2	22.2
Abortion, spontaneous	13	2	15.3	8	1	12.5	5	1	20.0
Term (viability)	47	2	4.2	21	2	9.5	26	0	
Died undelivered (previable)	9	9	100.0	9	9	100.0			
Still pregnant	1			1				0	
Unrecorded termination	13	8	61.5	13	8	61.5			
Total	145	40	27.5	105	37	35.2	40	3	7.3

A study of this table reveals some interesting facts. When pregnancy was terminated in the previable period the mortality rate was 28.3 per cent. In the patients receiving no vitamin therapy, the rate was 32 per cent and in the vitamin therapy series 22.2 per cent, the difference being practically negligible and indicating that abortion was perhaps done too soon in the latter series or that therapy was incomplete. When abortion was spontaneous, the mortality rate was 15.3 per cent in all cases, and 12.5 per cent and 20 per cent, respectively, in the nontreated and treated group. Here again, though the series is small, there is little or no difference, but definitely the mortality rate is lower than in the group of artificially terminated pregnancies.

In the 47 patients going to term, only two died, an incidence of 4.2 per cent, and both of them were in the nontreated group. Twenty-six patients received vitamin therapy and went to term with no fatalities in the group.

Early and effective therapy then is indicated and interruption of pregnancy is not indicated. From a study of the literature and from a careful review of a personal series, it is an opinion that interruption of pregnancy is definitely contraindicated, is fraught with danger, and is definitely a factor in the production of a higher mortality rate.

In an effort to determine what constitutes adequate therapy, the forty patients receiving vitamin therapy were studied. No uniform dosage or combination of various fractions of the vitamin complex or of other vitamin was used. That a large dosage of thiamin chloride is indicated is demonstrated by reviewing the personal series. The average daily dose of thiamin chloride in five cases was from 10 to 18 mg.; in Case 10, 80 mg. per day; and in Case 14, 132 mg. per day for seventeen days.

Matsen[47] and Behrman[20] both recommend 20 to 50 mg. of thiamin chloride daily, for at least two weeks. No harmful effect was noted from these larger dosages. Unfortunately no studies of excretion were done, so that the actual utilization of such large dosages cannot be ascertained. A clue as to the amount of thiamin chloride required daily is given in a recent case (U. H. 73607) of pernicious vomiting seen at the third month of pregnancy. The patient had all the typical signs and symptoms of a combined pellagra and scurvy without evidences of a polyneuritis. The blood pyruvic acid on admission was 3.7 mg. per cent, and although the patient was given 100 mg. of thiamin chloride daily, the pyruvic acid level did not reach 1.2 mg. per cent until the eighth day of therapy. The level then varied from 1.6 to 2.1 mg. per cent on a daily intake of 100 mg. thiamin chloride.

It seems reasonable that 10 to 15 mg. of thiamin chloride daily is a subminimal dose in these cases and that 50 to 100 mg. per day is necessary. This must, however, be reinforced with a diet high in other vitamins and

B complex as soon as the patient is able to take food. In some instances the addition of hydrochloric acid to promote digestion, and of an iron compound to combat anemia is necessary.

Passive motion of paralyzed extremities and proper splinting to combat deformities must also be done. The rate of recovery is slow. Improvement may be noted within a week but many patients do not regain full usage of the involved muscles until six to fifteen months have elapsed after the onset of therapy. This is emphasized in 40 cases in which the rate of recovery is mentioned. The recovery rate in months was not given in many instances but stated as "slow" or "long recovery." When the recovery rate was given it varied from two months to eighteen months, the average being 7.5 months.

Every patient who has nausea and vomiting should receive at least 1,000 units of thiamin chloride, and an adequate amount of B complex daily, taken at a time when the vomiting is least likely to occur. If this cannot be taken and retained orally then corresponding amounts should be given intramuscularly. This will prevent the appearance of the early signs of vitamin B deficiency, one of which is vomiting, and the development of polyneuritis which is a late sign of polyvitamin deficiency.

No definite conclusion has been reached as to the effect of vitamin B deficiency upon the fetus in utero. Intrauterine death does occur, and spontaneous abortion is not infrequent.

Uneo,[15] and Moore and Brodie[11] fed rats on a vitamin B deficient diet and noted abortions and absorption of the embryo, death of the young at birth or during the nursing period. The animals exhibited all the evidences of severe polyneuritis, and on autopsy there was found myelin degeneration of the phrenic and vagus nerves. Moore and Brodie report the case of a woman on a deficient diet who had a normal delivery and a post-partum hemorrhage. Although the baby appeared normal, it developed hemorrhages in the urine, became jaundiced, and died on the fifth day. Autopsy revealed many hemorrhagic areas, dilatation and hypertrophy of the right ventricle of the heart and myelin degeneration in the nerves. Careful examination of the 145 cases herein studied or reported failed to reveal post-mortem examinations of the fetus at any stage of gestation. This should be done in the future, for further study on this problem is necessary.

Vignes[16] regards vitamin B deficiency as frequently responsible for abortion, and ineffectual labors with post-partum hemorrhage and inertia uteri.

In the 26 women in the present study who received vitamin therapy, there was no recorded incidence of inertia uteri or post-partum hemorrhage. One infant was macerated at birth, all others were apparently normal infants. In the 21 women who continued the pregnancy to the period of viability, or to term without vitamin therapy, two were delivered by abdominal cesarean section, one by vaginal cesarean section,

and the remainder had normal deliveries, without any recorded evidence of inertia uteri or hemorrhage. The babies were all said to be normal living children.

There is insufficient evidence present in the protocols of the 47 women to make any statement as to the effect of the vitamin deficiency or vitamin therapy on lactation.

Stahler[12] estimated the amount of vitamin B_1 in the blood of four newborn children and found meager amounts of vitamin B_1 in the umbilical cord blood unless the mother received 10 mg. of vitamin B_1 shortly before delivery. The placenta, then, prevents no barrier to the passage of the thiamin from mother to child. Whether it also acts as a storehouse or reservoir is unknown. Dubrauszky and Lajos[3] found the vitamin B_1 level of the placenta higher than either the maternal or fetal blood levels. From their unconfirmed investigation it would appear that the placenta could act as a reservoir, giving the intrauterine fetus protection for a longer period of time in instances of maternal deficiency.

SUMMARY

1. Pernicious vomiting of pregnancy may result in a vitamin B deficiency with a severe polyneuritic syndrome.

2. Ocular symptoms which heretofore have not been stressed were present in 4 of 15 cases.

3. One hundred and thirty previously reported cases are reviewed with respect to vitamin therapy and maternal mortality, and 15 additional cases are reported.

4. If a polyneuritis develops 50 to 100 mg. of thiamin chloride should be given daily. No complications from these large doses have been observed.

5. Therapeutic abortion is definitely contraindicated, and if done increases the mortality rate.

6. Ultimate recovery is slow under the best of therapy and may require fifteen to eighteen months.

7. Further study is necessary to determine the effect of vitamin B deficiency on the fetus in utero in the human being. The same statement holds true in regard to the placenta.

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621 MEDICAL ARTS BUILDING

ETHER IN THE BLOOD OF THE NEWBORN INFANT

A Quantitative Study

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OBSTETRIC anesthesia may disturb the onset of respiration at birth by producing either (a) anoxia, or (b) anesthesia, or (c) both of these states. Thus, on the one hand (a), the oxygen supply of the mother's blood may be affected so as to diminish the amount of oxygen available to the fetus during the last critical moments when it is still dependent upon the placental circulation. Under such circumstances the infant may be born with the nervous control of respiration temporarily or permanently damaged by anoxia. Evidence has been put forward by various authors[1-3] to show that the onset of neonatal respiration may be disturbed in this way by the use of too much nitrous oxide gas, and perhaps during the administration of other anesthetic agents. On the other hand, (b) as might be expected, some anesthetic substances may themselves pass through the placenta and accumulate in the fetal blood in concentrations sufficient to render respiration shallow or delayed at birth from actual narcosis, despite adequate fetal blood oxygen levels. There are probably situations, (c) in which both the former and the latter disturbances affect the baby, but we have felt that delayed respiration or apnea, due entirely to the directly narcotizing effect of the anesthetic, was primarily the mechanism involved when babies were slow to breathe after delivery under ether. Although Eastman[1] found that in eight infants so delivered, the blood oxygenation was slightly below that expected in deliveries without anesthesia, a similar comparison in a somewhat larger series[4] showed the oxygen levels of babies delivered during ether anesthesia to be somewhat higher than the levels in the unanesthetized controls. Moreover the infants of this series who displayed some degree of apnea were not worse off for oxygen than were the others who breathed promptly.

In earlier papers the average amounts of nitrous oxide and of cyclopropane[4] in the maternal and the fetal blood at birth have been stated, but no figures have been found in the literature to indicate how much ether may enter the blood during the average delivery and how this is distributed between the maternal and fetal circulations. Because of this gap in our knowledge, and because we have reason to believe that any neonatal respiratory difficulty *assignable to the anesthetic* in deliveries under ether is usually a narcotic and not an anoxic phenomenon, it

seemed important to measure the amounts of ether actually present in the blood of the mother and of the infant in a considerable series of unselected deliveries.

METHODS

As soon as the infant was born, a section of the umbilical cord was isolated between two clamps. The contents of the umbilical vein and of the umbilical arteries in this isolated section thus represented the fetal arterial blood as it flowed from the placenta to the infant and the fetal venous blood returning to the placenta to be re-oxygenated; the isolation of this cord segment supposedly preserved these samples in the state obtaining immediately after birth. As soon as this length of cord could be removed to the laboratory, a sample was drawn from the umbilical vein, and from the arteries also if they contained sufficient blood. These samples were drawn into glass syringes in which oxalate, or heparin, and mercury were used to fill the dead space, as suggested by Adriani.[5] In many instances a specimen of venous blood was taken from the mother's arm at the exact time the cord specimen was isolated, or as near it as possible.

For a considerable period of time we attempted to use the iodine pentoxide method of Haggard[6] for the determination of ether in blood. This procedure proved unreliable in our hands, however, and we therefore gave it up in favor of the sulfuric acid dichromate method of Shaffer and Ronzoni.[7]

Clean outside air is slowly drawn over a 2 c.c. sample of the blood to be tested, thus vaporizing its ether content. This air is then bubbled slowly through 5 c.c. of concentrated sulfuric acid with the formation of ethyl sulfuric acid. The vaporization requires about two hours, and during the last half hour of this time the blood sample is immersed in a warm water bath to volatilize the last trace of ether. A measured amount of a standard bichromate solution is pipetted into the acid, the tubes being immersed in running tap water to prevent heating. The acid bichromate is then allowed to stand overnight to insure complete oxidation. An excess (2 to 4 Gm.) of potassium iodide is added with starch solution as an indicator. The liberated iodine is titrated against standard thiosulfate solution and the ether content of the 2 c.c. blood sample determined by a simple calculation. Repeated analyses for known amounts of ether added to blood have shown an accuracy, in our hands, of about 96 per cent for this method, as indicated by the results of trial assays in Table I.

TABLE I. ACCURACY OF METHOD. AMOUNT OF ETHER RECOVERABLE FROM SAMPLES OF KNOWN COMPOSITION

ETHER IN SAMPLE	ETHER RECOVERED		AVERAGE	PERCENTAGE
	TRIAL 1	TRIAL 2		
1. 2.13 Gm./liter	2.04	2.06	2.05	96.4
2. 3.40 Gm./liter	3.41	3.31	3.36	98.8
3. 7.71 Gm./liter	7.60	7.24	7.42	96.2

Since the placenta is a highly permeable barrier and should be particularly so for such volatile substances as ether no great difference was expected between the level of ether in the blood of a mother and in that

of her baby before the onset of neonatal respiration, although some individual variations were anticipated. Therefore, in the beginning of this work, it was puzzling to find the quantity of ether in the blood from the umbilical vein often considerably less than that in a specimen taken from the maternal vein at the moment when the cord was clamped. An explanation appeared when, at the suggestion of Dr. Charles C. Roby, we investigated the diffusion of ether through the walls of the umbilical vessels to the surrounding atmosphere during the few minutes elapsing from the time the cord was clamped until the time syringes were filled from its vessels in the laboratory. Since for various reasons it seemed wiser to use a collection process which necessitated this short interval, and since it was found that diffusion (with consequent lowering of the ether level in the cord vessels) did actually occur, a correction factor was devised. This was accomplished by measuring the ether in the vessels of umbilical cords obtained repeatedly from the same vessels at five-, ten-, and fifteen-minute intervals after the delivery. From the averages of such data, it was possible to project a curve for ether loss through the wall of the umbilical vein and a corresponding one for the umbilical arteries; reference to this curve and to the time elapsed between clamping the cord and sampling its contents allowed a reasonably accurate measurement of the original ether values by adding the resultant correction factor to the actual amount of ether in the sample. No such correction was needed for the maternal vein specimens, since they were drawn directly from the arm into the storage syringe. It was interesting that the correction factor for blood standing in the thin-walled umbilical vein proved to be larger (0.15 Gm. per liter of blood during five minutes) than that for blood in the thicker-walled arteries (0.12 Gm. for the same period). While delay in removing specimens from the vessels into the syringes did cause this predictable and correctable loss, it was found by repeated trials that once in the syringe the blood sample could be stored several hours, or overnight, if necessary, with only insignificant alterations in the amount of ether recoverable. Such a storage period was seldom required, as it was usually possible to collect the blood during the morning and to begin the chemical analyses immediately.

RESULTS

A general tabulation of the results from 68 infants and 58 mothers is presented in Table II. This enumerates a series of 66 deliveries (two with twins), in all of which at least one sample of cord blood, usually from the umbilical vein, was secured. At the majority of deliveries, a specimen from the maternal vein was also obtained; in somewhat less than one-half an umbilical artery specimen was available. In 22 deliveries with 23 infants, all three specimens were secured. The figures of Table II are perhaps more easily comprehended if spotted on a chart (Fig. 1), which shows the range over which the data spread, although it does not identify those maternal and fetal bloods which were obtained at the same delivery.

Several facts are apparent. The amounts of ether in the maternal venous and the umbilical vein (actually fetal arterial) bloods are scat-

TABLE II. ETHER, IN GRAMS PER LITER, IN MATERNAL AND FETAL BLOOD AT DELIVERY

TYPE OF DELIVERY†	ANESTHETIC			ONSET OF RESPIRATION*	UMBILICAL VEIN	UMBILICAL ARTERY
	TYPE	DURATION (MINUTES)	MATERNAL BLOOD			
1 N.D.	Closed		0.658	B	0.633	0.443
2 N.D.	Closed	25	0.724	A	0.789	0.489
3 L.F.	Closed	15	1.084	A	0.689	0.480
4 N.D.	Closed	12	0.667	A	0.744	0.489
5 N.D.	Closed		0.528	A	0.492	0.156
6 N.D.	Closed	16	0.848	A	0.743	0.610
7 L.F.	Closed	14	0.324	A	0.418	0.239
8 N.D.	Open	17	0.594	B	0.538	0.480
9 L.F.	Closed	20	0.658	A	0.585	0.378
10 N.D.	Closed	20	0.545	A-	0.510	0.000
11 L.F.	Closed	26	0.937	A	0.790	0.295
12 N.D.	Closed	22	0.722	A	0.558	0.220
13 N.D.	Closed	35	0.851	A	0.705	0.324
14 L.F.	Closed	35	0.927	A	0.970	0.656
15 N.D.	Closed		0.895	B-	1.030	0.439
16 L.F.	Open	50	0.556	B	0.558	0.371
17 L.F.	Closed		0.787	B	0.481	0.378
18 N.D.	Closed		0.292	A	0.603	0.423
19 N.D.) twins	Closed		0.949	C Case 1	1.104	0.360
20 N.D.)	Closed			C Case 2	1.492	0.462
21 L.F.	Open	23	0.292	A	0.603	0.463
22 N.D.	Closed	10	0.445	A-	0.488	0.248
23 L.F.	Closed		1.084	A	0.705	0.564
Average of 22:			0.698	Average of 23:	0.704	0.389
24 N.D.	Open		0.650	A	0.690	
25 N.D.	Open		0.844	A	0.706	
26 N.D.	Open		0.496	B	0.520	
27 N.D.	Closed		1.011	A	0.511	
28 N.D.	Closed		0.835	A	0.835	
29 N.D.	Closed		0.631	A	0.595	
30 N.D.	Closed		0.733	A	0.695	
31 L.F.	Closed		0.454	B	0.414	
32 L.F.	Closed	25	0.909	A	0.687	
33 N.D.	Closed	8	0.468	A	0.492	
34 N.D.	Open		0.786	A	0.873	
35 L.F.	Open		0.900	A	0.900	
36 N.D.	Closed	25	0.602	A	0.536	
37 N.D.	Open		0.528	A	0.492	
38 N.D.	Closed	19	0.742	A	0.797	
39 N.D.	Open		0.519	A	0.511	
40 N.D.	Closed	14	0.787	A	0.659	
41 N.D.	Closed	25	0.334	A	0.456	
42 N.D.	Closed	24	0.845	C	1.140	
43 Br.	Closed	20	0.897	B	0.880	
44 L.F.	Closed	27	0.482	C	0.660	
45 L.F.	Closed	20	2.030	C	1.143	
46 N.D.	Closed		0.555	A	0.511	
47 M.R.	Closed	20	0.900	C	0.790	
48 N.D.	Closed	20	0.437	A	0.464	
49 Br.	Closed	32	1.080	A	1.160	
50 N.D.	Closed	30	0.474	A	0.502	
51 N.D.	Closed	11	0.538	A	0.390	
52 L.F.	Closed	23	0.445	A	0.557	
53 N.D.	Closed	11	0.649	A	0.697	

*Onset of respiration: A, immediate; B, slightly delayed; C, delayed, required some resuscitation.

†Type of delivery: N.D., normal; L.F., low forceps; Br. breech; M.R., manual rotation.

TABLE II—CONT'D

| TYPE OF DELIVERY† | ANESTHETIC | | | ONSET OF RESPIRA-TION* | UMBILICAL VEIN | UMBILICAL ARTERY |
	TYPE	DURATION (MINUTES)	MATERNAL BLOOD			
54 M.R.	Closed		0.585	C	0.604	
55 N.D.	Closed	17	0.695	A	0.604	
56 N.D.	Open		0.343	A	0.520	
57 N.D.	Open		1.309	C	1.290	
58 L.F.	Closed		0.910	A	0.622	

Average of 57: 0.713   Average of 58: 0.692

TYPE OF DELIVERY†	ANESTHETIC			ONSET OF RESPIRA-TION*	UMBILICAL VEIN	UMBILICAL ARTERY
59 N.D.	Closed			A	0.474	0.232
60 L.F.	Closed			A	0.511	0.285
61 N.D.	Closed			A	0.233	0.298
62 N.D.	Closed			A	0.894	0.573
63 N.D.	Closed			A	0.659	0.248
64 L.F. twins	Closed			A	1.085	0.517
65				A	Case 1 0.511	Case 1 0.000
					Case 2	Case 2
66 N.D.	Open			A	0.547	0.415
67 L.F.	Open			A	0.530	0.260
68 N.D.	Closed			A	0.734	0.555

Average of 68: 0.681; of 33: 0.374

tered through a wide range of values, but their averages are very nearly identical at about 0.7 Gm. of ether/liter of blood. If, as on the spot chart, the extreme 10 percentiles are not included and the zones (shaded in the chart) occupied by the middle 80 percentiles are compared, it will be seen that they closely approximate one another, with the figures on the fetal side of the placenta a little higher than those for the maternal blood. Although this suggests a close relationship constantly maintained across the placenta, such a relationship is not borne out by determinations for individual mothers and their babies. Thus, at the delivery of Patient 3, for example, the maternal value was nearly 1.1 mg., the fetal less than 0.7, while in Case 27, the fetal value was about one-half the maternal. In other instances, such as Cases 15 and 19, the fetal blood contained much more ether than the maternal. Nevertheless, the average ether level for the infants of the 10 mothers having the most ether in their blood was 0.943, while in the infants of the 10 mothers having the least ether the corresponding figure was only 0.502. The ether present in blood returning to the placenta in the umbilical arteries was represented by a more compact group of figures, below those for the umbilical vein in proportion to the amount of ether which must have been absorbed by the fetal tissues, and yet to some degree overlapping the umbilical vein levels (Fig. 1). In 32 of the 33 infants on whom umbilical vein and artery specimens were both obtained, the amount of ether was less in the latter.

The comparison between maternal and fetal ether levels suggests an unstable and frequently changing situation which, nonetheless, tends

to be fundamentally consistent.   In an effort to check the effect of the varying conditions occurring during the progress of obstetric anesthesia, we examined two venous blood samples from the same woman at a five-minute interval shortly before the moment of birth.   Such figures, secured from 26 patients, are shown in Table III.   There was no regularity of results, so that the quantity of ether increased in the blood of 12 patients, decreased in that of 12 others, and remained the same in two. Such divergent findings, present because the patients were not saturated and thus stabilized with regard to ether, make it less surprising that the
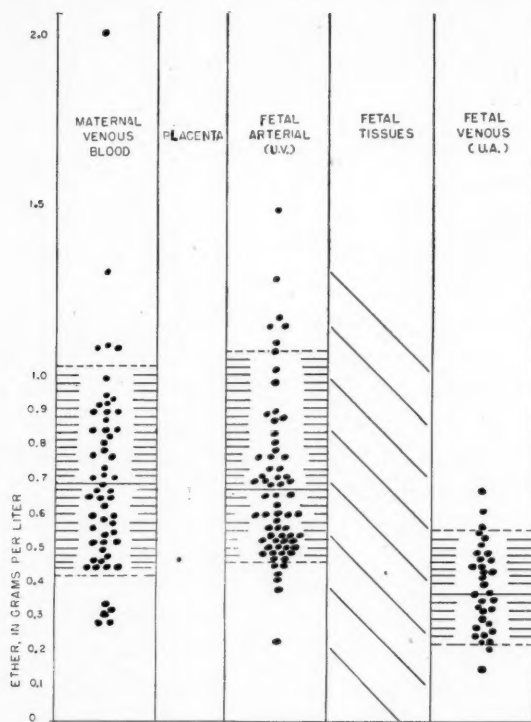
Fig. 1.—Amounts of ether in maternal and fetal blood at delivery, from the data of Table I.   Each dot stands for one specimen.   The solid horizontal line represents the average in each column; 80 per cent of the values fall within the shaded areas.

amounts of ether in maternal blood were so widely scattered at birth. With such variable and shifting ether values in the maternal circulation the amounts in the fetal blood might not simultaneously and exactly reflect each change on the maternal side of the placenta.   Nevertheless the quantity of ether reaching the fetus in the umbilical vein was roughly proportional to that in the mother's blood.   The general level lay between 0.45 and 0.90 Gm. of ether per liter of blood in samples from both these sources, nor was this influenced by the way in which the ether was administered (Table IV).

TABLE III. CHANGE IN ETHER IN MATERNAL BLOOD JUST BEFORE DELIVERY*

	TYPE OF ADMINIS-TRATION	ETHER IN VENOUS BLOOD	
		± 5 MINUTES BEFORE DELIVERY	AT DELIVERY
1	Closed	0.510 Gm./L	0.658 Gm./L
2	Closed	0.760	0.909
3	Open	0.909	0.786
4	Closed	0.900	0.724
5	Closed	0.620	0.580
6	Closed	0.500	0.845
7	Closed	1.204	0.897
8	Closed	0.667	0.667
9	Open	0.528	0.519
10	Closed	1.002	0.695
11	Closed	0.232	0.324
12	Closed	0.611	0.787
13	Closed	0.779	2.030
14	Closed	0.417	0.343
15	Closed	1.507	0.658
16	Closed	0.640	0.900
17	Closed	0.380	0.545
18	Closed	0.670	1.820
19	Closed	0.555	0.555
20	Closed	0.555	0.482
21	Closed	0.555	0.185
22	Closed	0.138	0.464
23	Closed	0.575	0.445
24	Closed	0.269	0.656
25	Open	0.547	0.510
26	Closed	0.796	0.910
Average 26:		0.647	0.727

*Amount of ether increased in 12.
Amount of ether decreased in 12.
Amount of ether unchanged in 2.

TABLE IV. EFFECT OF METHOD OF ADMINISTRATION AND OF PRE-ANESTHETIC RECTAL ETHER

ADMINISTRATION OF ETHER	NUMBER OF SAMPLES	SOURCE	ETHER GM./L (AVERAGE)
Open drop method	12	Maternal vein	0.651
	14	Umbilical vein	0.663
	5	Umbilical artery	0.398
Closed method	45	Maternal vein	0.732
	54	Umbilical vein	0.685
	28	Umbilical artery	0.369
Rectal ether as pre-anesthetic medication plus ether anes-thesia	10	Maternal vein	0.655
	11	Umbilical vein	0.682
	8	Umbilical artery	0.411

DISCUSSION

Goodman and Gilman[8] state that the presence of 1.0 to 1.1 Gm. ether per liter in the venous blood results in a state of light anesthesia. Most of the results in this study fell below this range, especially those for the infants, whose *venous* blood (that in the umbilical arteries) contained an average of only 0.37 Gm./liter, as against the average of 0.68 Gm. for their *arterial* blood. The significance of these figures emerges more

clearly if one reviews a few pharmacologic facts on the absorption and behavior of ether in the body. If air containing a constant percentage of ether is continuously administered to an experimental animal, the concentration of ether in the arterial blood rises more rapidly than that in the venous, the difference between the two being the amount of ether which is deposited in the tissues through which the blood has circulated. After a certain time the tissues become saturated so that no more ether can be taken up by them, then the venous and arterial levels become more or less equal. Robbins[9] has found this state to be brought about after from thirty to sixty minutes of ether administration while Haggard[10] published the protocol of an experiment in which the venous level was slightly below the arterial after as much as 120 minutes of

ARTERIAL AND VENOUS ETHER LEVELS COMPARED DURING INDUCTION
(0.2 GRAM ETHER PER LITER INSPIRED AIR) AND DURING RECOVERY
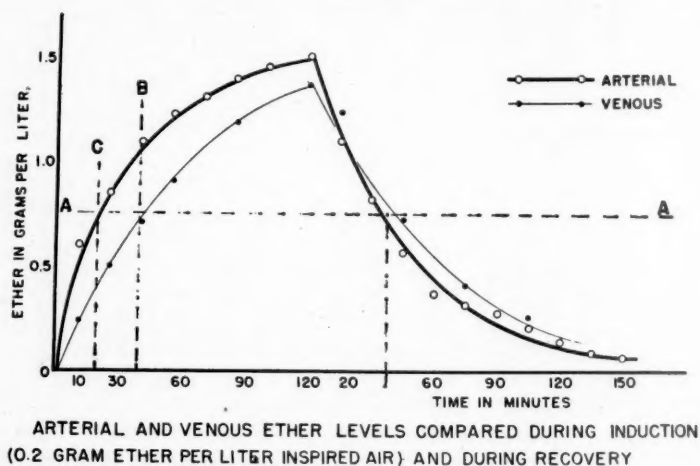
Fig. 2.—Data from experiment of Haggard presented and arranged in graphic form with his permission. The line $A \ldots A$ has been superimposed upon his data at the level of maternal venous and fetal arterial ether concentration as found in the present study. Line B indicates, in general, the maternal range; Line C, the fetal.

administration. The exact saturation point depends, obviously, on a number of factors such as the amount of ether in the respiratory mixture and the depth of breathing. After administration is stopped, elimination at once begins, with a gradient downward from the tissues via the veins to the lungs, so that while ether is being removed the amount in the veins is above that in the arteries.

This is graphically shown by the curved lines of Fig. 2, which has been prepared from Haggard's data obtained in the animal experiment mentioned above. The arterial level may be seen to be consistently above the venous until just after administration has ceased, when it falls below the venous curve. To illustrate the quantitative interrelationships of ether in the maternal and fetal bloods during delivery, certain general average figures from the present study have been indicated on the same diagram. The horizontal dotted line $A \ldots A$ is drawn at a

level of about 0.7 Gm. ether/liter, and thus indicates the amount in the venous blood of the average mother in the series. In general, one may expect that the average level in the maternal arterial blood must have been somewhere in the neighborhood of 1.1 Gm., since the vertical line *B* indicates that to have been the level in the experimental animal at the time the venous level was 0.7 Gm. At least the maternal arterial ether blood must lie above the venous. The dotted line *A . . . A* also represents the level of ether in the *arterial* blood of the fetus at birth, since such is the character of the blood coming from the placenta in the umbilical vein. If one drops another perpendicular line (*C*) on the diagram to denote an arterial level of 0.7 Gm. ether, the simultaneous venous level falls at about 0.35 Gm./L, and this agrees very well with our average figure of 0.37 Gm./L in the fetal venous (umbilical artery) specimens. In short, although it is true that ether administered to the mother reaches the fetus as well, it seems to do so at a considerably lower level. The beginnings of placental separation, or at least of impaired contact between uterus and placenta may have something to do with this relationship, and a certain amount of ether may be taken up in the amniotic fluid, as Dr. Irving[11] has suggested. The authors have not as yet determined how much of the ether reaching the placenta goes off in that direction and how much more may be absorbed by placental tissue itself. Any distribution of anesthetic to these regions must diminish that available for absorption by the fetal tissues. It is true, however, that just as prolonged administration tends to saturate the tissues of any subject and to bring venous and arterial levels closer to one another, so its effect in obstetrics would be to elevate the ether level in all parts of the fetus toward that of the mother, and thus to eliminate any advantage or protection accruing to the fetus in anesthesia of the usual duration. All of these statements must, of course, be made in the most general way, since cells differ in the rate at which they absorb ether, and nothing is known of the behavior of the fetal brain tissue, for example, in this regard.

TABLE V. ETHER CONCENTRATIONS IN THE VENOUS BLOOD OF MOTHERS AND THEIR INFANTS APPROXIMATELY THE SAME TIME AFTER DELIVERY

CASE	HOURS AFTER DELIVERY	GRAMS ETHER PER LITER BLOOD	
		MATERNAL VENOUS	INFANT'S VENOUS
1	1¾	0.416	0.371
2	2	0.268	0.268
3	2	0.324	0.185
4	2	0.278	0.167
5	2	0.370	0.278
6	2	0.370	0.093
7	2	0.370	0.232
8	1¾	0.000	0.362
9	1½	0.093	0.000
10	1¾	0.371	0.093
11	2½	0.000	0.000
12	2½	0.139	0.093
13	1½	0.240	0.139
14	2	0.208	0.278
15	2	0.139	0.111
16	3	0.009	0.000
Average of: 16		0.275	0.167

Some evidence has been obtained to show that after the administration of ether is stopped the fetus probably eliminates it as rapidly as does the mother. Table V shows that an hour or two after delivery samples obtained simultaneously from the mother's and the infant's veins usually show a smaller amount in the latter specimen. Whether or not an extra quantity was administered to the mother after delivery for purposes of episiotomy repair, the favorable position of the infant thus after as well as during birth is apparent from these data. The respiratory minute volume of the infant is much greater per unit of body mass than that of the mother, which gives a decided advantage to the infant in clearing a volatile anesthetic from the blood stream. It is, of course, possible that the fetus and newborn infant may respond more sensitively than the adult organism to small quantities of ether; no observations are available on this point. That the anesthesia does affect the fetus and newborn infant sufficiently to produce some sluggishness of response must be accepted, but the degree of actual hazard requires some discussion and qualification.

Every writer on neonatal apnea mentions direct anesthesia as one of several jeopardizing factors, but we have encountered only four attempts to secure quantitative measurements bearing upon the ether problem in obstetrics. Two of these, concerned largely with the oxygen relationships of ether anesthesia, have been mentioned above.[1, 4] Another study, that of Cole, Kimball, and Daniels,[12] used the very practical and simple method of timing the interval between delivery and respiratory onset in a large series of infants, and of noting the circumstances under which important delay occurred. The evidence obtained showed that ether had a definite effect in delaying the onset or disturbing the depth of respiration after birth, and that these effects increased in severity the longer the anesthetic had been administered. A striking thing shown by Cole, Kimball, and Daniels was the large percentage of severe apnea resulting when ether had to be given for more than thirty minutes, although by contrast with deliveries under nitrous oxide the effects of ether were comparatively moderate. One must accept the general evidence presented in that study as confirming fairly frequent clinical encounters with sleepy newborn infants, smelling of ether and breathing shallowly, although with fair regularity. It should be noted, however, that this is a self-righting condition, as with every breath the infant exhales he is getting rid of his ether load, so that this sort of infant almost always has a better prognosis in the nursery than does one whose respiratory sluggishness and irregularity is the consequence of an episode of anoxia. Apnea due to anesthesia is not deleterious until after birth, by which time the administration is over and elimination begun, whereas anoxial disturbances can and do involve the fetus in utero as well as the infant after birth.

The other study of interest was made by Rosenfeld and Snyder[13] upon fetal animals whose mothers were given various sedatives and anesthetics. The fetal movements of respiration were suppressed during

administration of most of these substances to the mother, often before surgical anesthesia was brought about in the maternal animal. This was the case in the observations with ether. The application of these studies to obstetrics and pediatrics is in some doubt until it can be shown that all fetuses including the human being make such movements normally and "physiologically," and certain questions have recently been raised upon that point.[14]

Our own observations agree with those just discussed in demonstrating that hesitation in respiratory onset does occur in some human infants whose mothers are anesthetized with ether and is correlated with the amount of ether reaching the fetus, which is in turn related to the amount in the maternal circulation. In Table II, the onset of respiration has been characterized by letters A, B, and C to indicate, respectively, immediate respiration, slight delay, and delay calling for resuscitation usually of a simple variety. Table VI presents the average

TABLE VI. RELATIONSHIP OF AMOUNT OF ETHER TO ONSET OF RESPIRATION

STATE OF INFANT	(A) BREATHED AT ONCE	(A-, B, C) BREATHING DELAYED	(C) REQUIRED RESUSCITATION
Maternal vein	0.684 Gm. (40)*	0.789 Gm. (17)	1.015 Gm. (7)
Umbilical vein	0.643 Gm. (50)	0.793 Gm. (18)	1.028 Gm. (8)
Umbilical artery	0.387 Gm. (23)	0.243 Gm. (9)	0.422 Gm. (2)

*Figure in parentheses represents number of samples.

figures, first in all deliveries resulting in babies breathing at once, second, in all other deliveries, and third, in the eight deliveries after which the infants required resuscitation. The increase as one passes from each of these categories to the next is very apparent as is the relationship between the maternal vein and umbilical vein averages in each group. The small number of figures for umbilical artery blood makes the averages of that group of no statistical value. Thus, while as stated at the beginning of this paper, no anoxial element is responsible for apnea in the newborn delivered under ether, there is a definite effect traceable to the anesthetic as such. Should breathing begin after only brief hesitation due to this cause, as is usually the case, the anesthetic in the infant's blood will have done no harm and will be eliminated. On the other hand, should the baby be sufficiently anesthetized so that the respiratory onset is more than slightly delayed, then the element of anoxia does become present, and increases.

Finally, before drawing conclusions, it must be emphasized that there are many other aspects by which the suitability of ether as an obstetric agent may be considered besides those described above. No attempt has been made here to discuss other factors than (1) the comparatively safe margin of oxygen supply in the obstetric use of ether, and (2) the degree to which ether itself may be expected to appear in the maternal and fetal blood during more or less routine deliveries.

CONCLUSIONS

1. In a series of 68 deliveries, the concentration of ether in blood from the umbilical vein was 0.681 Gm. per liter. The average in the venous blood of the mothers of 58 of these infants was 0.713 Gm. per liter. In 33 infants the umbilical arteries contained blood with an average ether content of 0.374 Gm. per liter.

2. The relationship between maternal and fetal ether levels was generally, although not always individually, a directly proportional one.

3. The low amounts in the umbilical artery blood suggest that the fetal tissues receive less ether than do the maternal.

4. Maternal and fetal ether levels were not influenced consistently by the type of administration nor by the use of rectal ether as a preanesthetic medication.

5. The blood of infants breathing at once, and that of their mothers, contained considerably less ether than did that of infants and mothers at deliveries associated with neonatal apnea.

6. Thus, ether administered to the mother during delivery may produce delay in the onset of respiration in the newborn infant. Ordinarily, this is not due to interference with the maternal and fetal oxygen supply but to the presence of ether in the fetal blood and tissues.

7. The comparatively large minute volume of respiration in newborn infants favors the rapid elimination of ether.

8. The relationship between apnea due to anesthesia and that due to anoxia is briefly discussed.

While this paper was in press, a communication appeared from Potter and others,[15] presenting figures for the amounts of ether in the venous blood of patients under that anesthetic. The averages ranged from 0.87 to 1.13 Gm./L. in various groups of patients.

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THE USE OF ERGONOVINE IN THE PLACENTAL
STAGE OF LABOR*

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THE third stage of labor is probably the most important phase of parturition. Notwithstanding the fact that it occupies an insignificant period of time in the many hours devoted to labor, this short period is packed with many hazards for the mother, real and potential. Post-partum hemorrhage contributes appreciably to maternal mortality. Even more important than the immediate blood loss is the increased hazard of infection introduced by the manipulations necessary to control the bleeding and fostered by the decreased effectiveness of the defensive mechanism as a result of the blood loss. Much of the morbidity or mortality directly attributable to the third stage of labor is never credited to this period.

It is almost a century since Credé studied the mechanism of placental separation and expulsion and suggested his method of management to reduce the high incidence of complications. Many modifications of the Credé method have been tried and found wanting during the intervening years. The introduction of oxytocic drugs led to their immediate adoption in the conduct of this period. However, this new measure failed to decrease the hazards of the third stage to any great extent. The vast majority of clinical teachers prefer not to interfere with this phase of labor, allowing the normal mechanism to operate. This is sound obstetric teaching.

During the past several decades, a number of new factors have entered into the conduct of labor which have seriously affected the course of the third stage. An ever increasing number of patients are confined in hospitals in which natural delivery is decreasing in frequency. Labor is often terminated in the primipara by the combined use of outlet forceps and episiotomy. These advantages necessitate the use of anesthesia. The pain of labor is relieved by various analgesic agents, which are sometimes carried to great extremes in order to eliminate the last shreds of discomfort inherent in physiologic parturition. Analgesia, anesthesia, and the increased incidence of operative procedures all combine to interfere with the normalcy of the third stage, thereby increasing the incidence of complications in this period. It becomes apparent that the

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normal mechanism of the third stage may no longer function safely in many cases, so that it may be necessary to resort to new measures in an attempt to safeguard this critical period in the same way that the other phases of the labor have been safeguarded.

Natural as well as artificial forces may produce an abnormal mechanism in the third stage. Long and difficult labor may reduce the effectiveness of the uterine contractions thereby interfering with a rapid and complete placental separation. The overdistention of the uterine cavity as a result of a large baby, the occurrence of multiple births, or an excessive amount of amniotic fluid may decrease the uterine muscle irritability and contractility and thereby affect normal uterine action. Inherent defects in the innervation or character of the uterus, about which we are only vaguely cognizant, may lead to an abnormal third stage mechanism. These are examples of failures in the normal physiology of reproduction which must be corrected if we are to prevent serious accidents.

The normal mechanism of the placental stage consists of two distinct phases, separation and expulsion. One cannot and should not initiate the latter until the former is completed. The first phase involves a slow, progressive separation of the placenta from the uterine wall and is brought about by physical changes that take place on the evacuation of the uterine cavity by the fetus.

The placenta normally remains attached to the uterus until the expulsion of the fetus. The sudden diminution in size of the uterine cavity results in a reduction of the surface area of the uterine wall to which the placenta is attached. The semi-rigid, noncontractile placenta cannot alter its surface area, and thus it partially or completely separates from its attachment. The speed with which the reduction of uterine surface area is accomplished determines the completeness of the separation. The initial reduction in the area of the placental site rarely results in complete separation for this process is far too slow and too ineffective. Bleeding occurs at this time behind the placenta but it is doubtful if the accumulated blood clot aids the separation by acting as a wedge. The retroplacental clot is not necessary in the mechanism of separation. In most instances it accumulates as a result of an incomplete separation or after the placenta is separated off the placental site while its expression from the lower uterine segment and vagina has been delayed. Uterine contractions now recur which shear the remainder of the placenta from its attachment. How effective a placental separation is depends on uterine contractility. Many variations in the character of the separation can and do occur. Generally, the longer the third stage lasts, the less complete the placental separation is and the greater the blood loss may be during this period.

It has been recognized from clinical experience that any interference with placental separation is likely to result in an abnormal third stage.

Premature attempts to induce separation by inciting uterine contractility by manipulation of the uterus may well result in an incomplete separation and excessive bleeding. Such uterine stimulation often provokes arrhythmic contractions or localized uterine irritability which interferes with normal placental separation. Premature attempts at expulsion often lead to an increased venous engorgement of the uterus or to the incarceration of an incompletely separated placenta within the contractile zone. To retain the normalcy of the third stage, it is most important not to interfere with the separation phase and to recognize when this phase is complete so that the expulsion of the placenta may be aided.

The use of an oxytocic drug in the third stage of labor was introduced as a means of facilitating the phase of separation in the third stage mechanism, thereby decreasing the hazards of this period. Pituitary extract has been used routinely for many years at the end of the second stage at the Chicago Lying-in Hospital. Its parenteral administration, however, rarely affected the phase of placental separation, for this route of drug administration results in a delay of six or seven minutes in the effectiveness of the drug. Usually separation is completed by natural forces in this period, and the effect of the oxytocic drug is to stimulate the uterus to expel the separated placenta into the distended lower uterine segment and vagina from which it may easily be expressed. Rarely, the oxytocic action occurs before the expulsion of the placenta from the contractile upper segment of the uterus or before separation is complete, in which event the placenta may be incarcerated firmly in this contractile zone. Such an undesirable complication may result in excessive bleeding and complicate placental removal in the event that it is indicated. This hazard decreases the value of this mode of therapy for the third stage.

Since the advent of ergonovine in 1935, further uses for this powerful oxytocic drug have been under investigation. Extensive pharmacologic and physiologic studies have amply demonstrated its profound oxytocic character, its prolonged effect, and the absence of undesirable reactions regardless of the mode of administration. Our early studies indicated that the oral and intramuscular routes were slow in their action, six or eight minutes elapsing from the time the drug was administered to the onset of activity. Intravenously administered, the drug exhibits activity within twenty or thirty seconds. The character of the response varies to some degree with the mode of administration (Fig. 1). When ergonovine is administered orally or subcutaneously, the initial uterine contractions are of moderate intensity and slowly increase in severity over a period of five or six minutes until they reach their maximum intensity. At the same time, there is a progressive increase in uterine tone which reaches its maximum state at the time of the greatest uterine action. This characteristic response to ergot preparations has made the

administration of the drug in the third stage of labor prior to the delivery of the placenta undesirable.

The intravenous administration of ergonovine is followed by a sudden uterine contraction of maximum intensity and tone. Contractions of low amplitude now begin and slowly increase in degree. Uterine tone, however, is maintained and diminishes slowly as the magnitude of the contractions increases. This unique response to the intravenous use of the drug has made possible its adoption in the placental separation phase.

If the phase of placental separation is entirely a physical phenomenon and the result of a sudden reduction of surface area of the placental site, then theoretically, the more rapidly this reduction takes place, the more
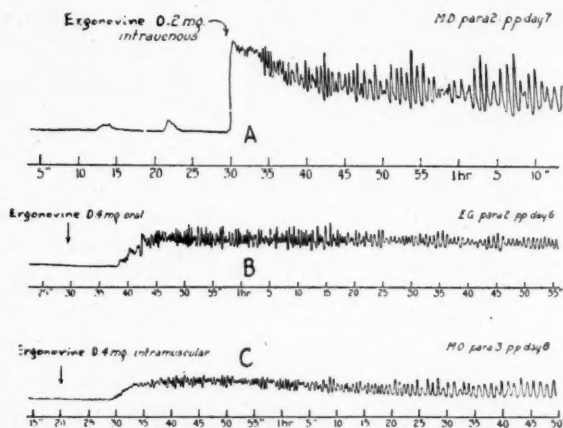
Fig. 1.—Kymographic tracings of uterine motility, showing the action of ergonovine on post-partum uteri by (A) intravenous, (B) oral, and (C) intramuscular administration. Note the immediate response of the drug following intravenous administration and the delay of only six to eight minutes following its oral and intramuscular use. The tetany is well maintained, and as it subsides increasingly vigorous contractions occur. The activity of the drug lasts two hours or longer.

complete will be the separation. There should be less likelihood of portions of the placenta remaining attached and thus complicating the third stage. To accomplish this immediate contraction of the uterus following the birth of the baby, 0.2 mg. of ergonovine (ergotrate H, Lilly) is given intravenously after the head is delivered and as the anterior shoulder is brought into view. If at this point, one allows twenty or thirty seconds to elapse for the drug to exert its action, the baby can be delivered. The uterus contracts almost instantaneously, separating the placenta cleanly from its attachment and pushing it out into the lower uterine segment and vagina (Figs. 2, 3, and 4). Palpation of the corpus uteri at this time will reveal it to be globular and firm. The placenta may now be expressed from the vagina. This management of the third stage artificially controls the phase of separation, whereas an oxytocic drug

administered intramuscularly after the baby is born prepares the way for a more favorable phase of expulsion.

In the expression of the placenta, several safeguards must be exercised. The corpus uteri must be in a contracted state before expression begins.
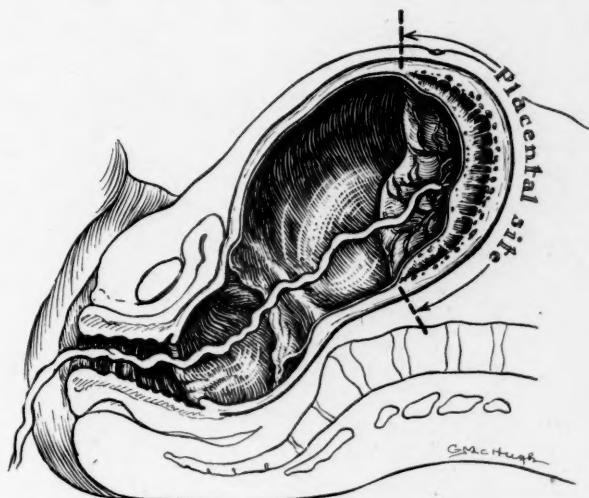
Fig. 2.—Showing the normal uteroplacental relationships when the cavity of the uterus is distended with the fetus. Note the length of the placental site indicative of its surface area and the characteristic discoid shape to the uterus.
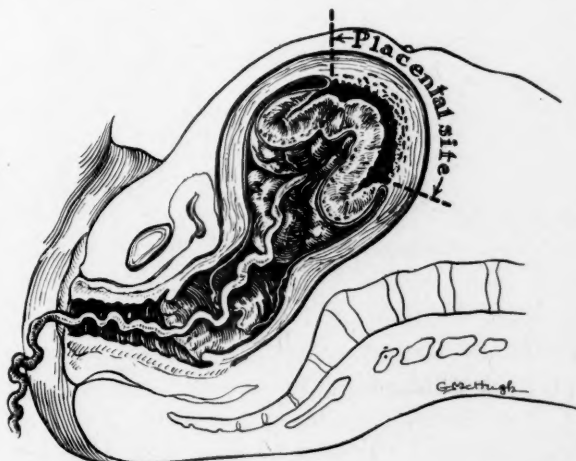
Fig. 3.—Showing the uteroplacental relationships immediately after the baby has been expelled from the uterus and the placenta has separated from its uterine attachment. Note the great decrease in surface area of the placental site, the thickened uterine wall and the change in uterine contours.

The entire uterus must not be pushed downward into the pelvis because this dislodgement leads to excessive bleeding. The venous return is shut off and the uterine sinuses become distended with blood, thereby tending

to increase the blood loss. Pastore has suggested a method to prevent this undesirable complication, but his method is not applicable when the attendant is conducting the labor without help. The left hand is placed flat on the abdomen with the fingers directed under the symphysis, thereby preventing the uterus from entering the pelvis while the right hand expresses the placenta. The same end can be accomplished by the accoucheur if he will make pressure with the fingers of the left hand just above the symphysis while the right hand pushes down on the corpus uteri. When the placenta is visible at the introitus, slight traction on the cord will deliver it most easily. However, traction on the cord is to be seriously condemned under any other conditions, for such manipulation on an incarcerated or partially adherent placenta may result in inversion of the uterus.
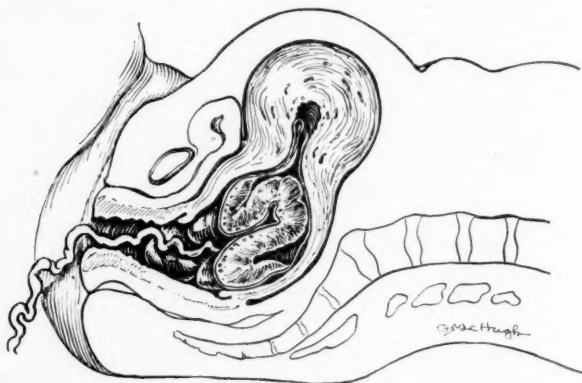

Fig. 4.—Showing the uteroplacental relationships after the expulsion of the placenta into the lower segment and vagina. The fundus of the uterus has become globular and has risen; the lower segment is distended by separated placenta.

The advantages of the method described lie chiefly in the marked reduction in the loss of blood and the freedom from complications of the third stage with their associated post-partum hemorrhage. The method has proved so effective on our service that the incidence of serious postpartum bleeding has been greatly reduced. The regime described is applicable only to institutional practice, for it requires someone to give the drug intravenously at the proper moment. Exact timing in the administration of intravenous ergonovine is most essential. There have occurred a few instances of incarceration of the placenta in the contracted zone, but this complication is not troublesome in an institution. The conduct of the third stage described should have particular appeal where patients are predisposed to abnormal uterine bleeding because of a previous post-partum hemorrhage, an excessively distended uterus, a long labor, or difficult operative interventions.

Since Jan. 1, 1938, it has been possible to make careful observations of the third stage of labor in 2,006 patients who had received ergonovine. The duration of the third stage, the blood loss and unusual complications were carefully recorded in each instance. Other factors in the labor and delivery which could influence the third stage were carefully analyzed. The uterine blood loss was measured after careful collection in a basin during and after delivery of the placenta. Bleeding from the episiotomy or perineal lacerations was excluded so far as possible. Since some of the blood from these sources inevitably went into the basin, the figures probably represent a higher loss than actually occurred from the uterus. This error is constant for the several groups of patients studied so that the results are comparable.

The most important part of this study concerns itself with the intravenous use of ergonovine after the head has been delivered and when the easy egress of the shoulders from the birth canal is assured. Two other groups of patients are presented. In both instances, placental separation and expulsion were accomplished by natural forces, following which ergonovine was administered intravenously to the first group and intramuscularly to the second group. All three of these groups are not quite comparable, for ergonovine was used in the second stage whenever there was an increased likelihood of an abnormal placental stage. Furthermore, ergonovine was administered intravenously in all patients in whom the placental stage was prolonged, abnormal, or complicated by an excessive blood loss. The third group of patients who received the drug intramuscularly, represented the patients who had the most normal natural third stage and the drug was given primarily to assure good uterine tone, thereby preventing excessive blood loss.

Table I presents a summary of the three groups of patients in whom ergonovine was used. More than half of the entire group, 1,020 patients, or 50.8 per cent of the total, received the drug during the second stage of labor as described previously. Of this group, 81 per cent of the patients had a measured blood loss of less than 100 c.c. and only 19 per cent lost more than 100 c.c. There were only 4 patients in whom the blood loss was more than 500 c.c., an incidence of less than one-half of 1 per cent. In the group of patients where ergonovine was administered intravenously after the placenta had been expelled from the uterus, 35 per cent lost not more than 100 c.c. of blood, whereas 65 per cent lost more than 100 c.c. It is worthy of note that although this represented a smaller group of patients, 753, there were 15 patients who had a blood loss of over 500 c.c., an incidence of 2 per cent. In the third group of patients in whom ergonovine was administered intramuscularly at the end of the third stage, 46 per cent lost not more than 100 c.c. of blood. There were 5 patients in whom the measured blood loss was more than 500 c.c., an incidence of 4.6 per cent. The striking fact in this résumé is the small blood loss during the third stage of labor in those patients who received ergonovine intravenously in the second stage of labor with the delivery of the shoulders of the baby. There is no comparison

TABLE I. BLOOD LOSS OF THIRD STAGE

	25 C.C.	50 C.C.	100 C.C.	200 C.C.	300 C.C.	500 C.C.	OVER 500 C.C.

Ergonovine Intravenously in Second Stage

(1,020 cases or 50.8% of total)

	25 C.C.	50 C.C.	100 C.C.	200 C.C.	300 C.C.	500 C.C.	OVER 500 C.C.
Primiparas	41	170	239	101	12	7	2
Multiparas	84	136	158	56	8	4	2
Total	125	306	397	157	20	11	4
Per cent	12	30	39	15	2	1	0.3

81 per cent of these patients lost not more than 100 c.c. of blood (measured), *19 per cent* lost more than 100 c.c., and *4 per cent* lost more than 200 c.c.

Ergonovine Intravenously in Third Stage

(753 cases or 37.5% of total)

	25 C.C.	50 C.C.	100 C.C.	200 C.C.	300 C.C.	500 C.C.	OVER 500 C.C.
Primiparas	6	14	59	129	55	36	5
Multiparas	17	52	117	152	63	38	10
Total	23	66	176	281	118	74	15
Per cent	3	9	23	37	16	10	2

35 per cent of these patients lost not more than 100 c.c. of blood (measured), *65 per cent* lost more than 100 c.c., and *28 per cent* lost more than 200 c.c.

Ergonovine Intramuscularly in Third Stage

(233 cases or 11.7% of total)

	25 C.C.	50 C.C.	100 C.C.	200 C.C.	300 C.C.	500 C.C.	OVER 500 C.C.
Primiparas	3	5	18	24	7	9	1
Multiparas	6	26	48	49	20	13	4
Total	9	31	66	73	27	22	5
Per cent	4	13	29	31	12	9	2

46 per cent of these patients lost not more than 100 c.c. of blood (measured), *54 per cent* lost more than 100 c.c., and *23 per cent* lost more than 200 c.c.

between the third stage in this group of patients and the two groups in whom the use of an oxytocic drug was delayed until after the third stage was complete.

The length of the third stage was much shorter than normal when ergonovine was used at the end of the second stage of labor. Of the total group of 1,020 patients, the third stage was one minute or less in 131, two minutes or less in 369, three minutes or less in 237 (Table II). Thus in 754 cases, or 73 per cent of the entire group, the placenta was delivered in less than three minutes. This confirms the impression that

TABLE II. LENGTH OF THE THIRD STAGE AND BLOOD LOSS

MINUTES	TOTAL CASES	% OF TOTAL	UNDER 200 C.C.	UNDER 50 C.C.	50 TO 99 C.C.	100 TO 199 C.C.	200 TO 299 C.C.	300 TO 499 C.C.	500 C.C.+
Ergonovine Intravenously in the Second Stage—1020 Patients									
3 or less	754	73	98%	335 45%	310 41%	92 12%	8 1%	7 1%	2 0.3%
4-10	237	23	94%	79 37%	84 35%	51 22%	10 4%	2 1%	1 %
11-30	22	2	77%	5 23%	2 9%	10 45%	2 9%	2 9%	1 5%
Over 30	7	1	100%	2 28%	1 14%	4 57%	0 0%	0 0%	0 0%

the separation of the placenta is almost instantaneous, occurring immediately after the passage of the fetus from the uterine cavity, and promoted by the oxytocic effect of the intravenous ergonovine.

There was a direct relationship between the blood loss and the length of the third stage. Thus, 98 per cent of the patients in whom the third stage lasted three minutes or less lost less than 200 c.c. of blood. In many instances the blood loss was infinitesimal in amount as can be noted in Table I. In only 7 patients was the duration of the placental stage longer than thirty minutes, and it is interesting to note that in all of these instances the blood loss was less than 200 c.c. A delayed third stage of labor, following the intravenous administration of ergonovine at the end of the second stage, is not necessarily associated with an increased blood loss.

TABLE III. LENGTH OF THE THIRD STAGE AND BLOOD LOSS

MINUTES	TOTAL CASES	% OF TOTAL	UNDER 200 C.C.	UNDER 50 C.C.	50 TO 99 C.C.	100 TO 199 C.C.	200 TO 299 C.C.	300 TO 499 C.C.	500 C.C.+
Ergonovine Intravenously in the Third Stage—753 Patients									
3 or less	202	27	78%	26 13%	49 24%	84 42%	22 11%	20 10%	1 0.5%
4-10	439	59	72%	52 12%	102 23%	167 37%	76 17%	35 8%	7 2%
11-30	93	13	62%	10 11%	20 22%	27 29%	18 19%	13 14%	5 5%
Over 30	11	0.1	27%	0 0%	0 0%	3 27%	2 18%	4 36%	2 18%
Ergonovine Intramuscularly in the Third Stage—233 Patients									
3 or less	37	15	89%	11 30%	13 35%	9 24%	3 8%	0 0%	1 3%
4-10	155	66	78%	23 15%	45 29%	52 34%	17 11%	15 10%	3 2%
11-30	40	17	66%	6 16%	8 20%	12 30%	7 18%	6 15%	1 3%
Over 30	1	0.4	0%	0 0%	0 0%	0 0%	0 0%	1 100%	0 0%

Table III presents an analysis of the group of patients who received ergonovine intravenously at the end of the placental stage. The effect of the oxytocic drug is demonstrated by the low incidence of post-partum hemorrhage. In more than one-half of the patients in this group, the placental stage lasted longer than four minutes. There was a greater average blood loss than in the preceding group.

Table III likewise presents a summary of the patients who received ergonovine intramuscularly at the end of the placental stage. In the majority of these patients, the length of the placental stage exceeded four minutes. The incidence of post-partum hemorrhage is not great in this group because of the fact that the drug was used intramuscularly only in the patients who had a normal third stage. Where the third stage was abnormal and a tendency to bleeding existed, the drug was administered intravenously. One can conclude that the length of the third stage determines to some extent the blood loss during this period.

Table IV is a summary of the labors in the group of patients who received ergonovine. It will be noted that 163 patients had a natural

TABLE IV. DELIVERY AND BLOOD LOSS

	TOTAL CASES	UNDER 200 C.C.	UNDER 50 C.C.	50 TO 99 C.C.	100 TO 199 C.C.	200 TO 299 C.C.	300 TO 499 C.C.	500 C.C.+
Intravenous Second Stage								
Natural	163	100%	90	61	12	0	0	0
Natural with episiotomy	307	97%	130	121	46	6	2	2
Low forceps	469	96%	183	183	84	13	5	1
Midforceps	64	91%	24	27	7	1	4	1
Breech	8	100%	2	4	2	0	0	0
Dührssen's	15	93%	1	10	3	0	1	0
Intravenous Third Stage								
Natural	271	83%	55	84	83	26	18	5
Natural with episiotomy	304	71%	19	69	130	50	27	9
Low forceps	96	59%	9	8	40	24	15	0
Midforceps	9	0%	0	0	0	2	7	0
Breech	62	73%	6	15	24	12	5	0
Dührssen's	1	0%	0	0	0	1	0	0
Intramuscular Third Stage								
Natural	86	83%	23	28	20	8	6	1
Natural with episiotomy	114	79%	12	32	46	13	11	0
Low forceps	26	51%	3	6	4	5	4	4
Midforceps	0	0%	0	0	0	0	0	0
Breech	7	72%	2	0	3	1	1	0
Dührssen's	0	0%	0	0	0	0	0	0

delivery unassisted in any way. This represents the most normal group of patients who received ergonovine intravenously just before the shoulders were delivered. In all instances the blood loss was less than 200 c.c. and in 93 per cent of this entire group less than 100 c.c. This group provides additional evidence of the diminished blood loss which follows this conduct of the placental stage. The type of delivery does not appear to have any great effect on the blood loss during the third stage of labor.

The intravenous administration of this drug at the end of the second stage was not successfully carried out in breech delivery. It is probably unwise to administer the drug before the baby is completely delivered. Should a premature contraction occur while the aftercoming head is still within the pelvis, great difficulty might be encountered in its delivery. For this reason, it is suggested that in breech delivery ergonovine be given intravenously after the birth of the baby and after the completion of the delivery of the placenta.

Of 16 patients who were delivered after Dührssen's incisions on the cervix, 15 received ergonovine with the delivery of the shoulders. It is of interest that in 14 of these the blood loss was less than 200 c.c. and in only one instance was the blood loss 500 c.c. Anyone who has had experience with this operation, which is usually combined with a difficult forceps, will realize that this result is in marked contrast to the usual experience. Prior to the use of ergonovine, it was necessary to resort to uterine tamponade in about one-third of the patients in whom

Dührssen's incisions were performed because of the prolonged and troublesome bleeding from the uterine cavity.

Table IV likewise presents a résumé of the type of delivery in the patients who received ergonovine intravenously or intramuscularly after the placenta was delivered. The blood loss was appreciably greater in both of these groups than in the former group, and the incidence of post-partum hemorrhage was increased. The type of delivery affected the blood loss only moderately.

Table V presents an analysis of the length of labor in relation to the blood loss during the third stage of labor. It is interesting to note that in 231 patients with short labors who received ergonovine with the delivery of the shoulders the blood loss was less than 200 c.c. in all instances. This is another striking example of the value of ergonovine administered at the end of the second stage of labor. In the group of patients in whom the labor was of average length, the blood loss was less than 200 c.c. in 95 per cent of the patients, whereas in 142 patients in whom the labor was long, the blood loss in 97 per cent was less than 200 c.c. The length of labor did not increase the blood loss nor the incidence of a pathologic third stage in this group.

TABLE V. LENGTH OF LABOR AND BLOOD LOSS*

	TOTAL CASES	UNDER 200 C.C.	UNDER 50 C.C.	50 TO 99 C.C.	100 TO 199 C.C.	200 TO 299 C.C.	300 TO 499 C.C.	500 C.C.+
Intravenous Second Stage								
Short	231	100%	99	99	33	0	0	0
Average	640	95%	283	232	97	18	7	3
Long	149	97%	49	66	27	2	4	1
Intravenous Third Stage								
Short	176	74%	22	39	69	21	20	5
Average	517	72%	60	120	193	85	50	9
Long	60	71%	7	17	19	12	4	1
Intramuscular Third Stage								
Short	62	75%	8	22	17	6	7	2
Average	160	79%	32	42	53	18	12	3
Long	11	46%	0	2	3	3	3	0

*Short labor: Primipara, less than 8 hr. Multipara, less than 4 hr.
Average Labor: Primipara, less than 24 hour. Multipara, less than 18 hr.
Long labor: Primipara, more than 24 hr. Multipara, more than 18 hr.

Table V likewise presents a résumé of the length of labor as it affected the third stage when ergonovine was administered intravenously and intramuscularly after the placenta had been delivered.

TABLE VI. MANUAL REMOVAL OF THE PLACENTA
(25 instances in 2,006 patients)

ERGONOVINE ADMINISTERED	NO. OF CASES	MANUAL REMOVAL	INCIDENCE	BLOOD LOSS (AVERAGE)
Intravenously second stage	1020	8	1:127	200 c.c.
Intravenously third stage	753	15	1:50	393 c.c.
Intramuscularly third stage	233	2	1:116	400 c.c.

Table VI presents the incidence of manual removal of the placenta in the entire group. It will be noted that the incidence of manual removal was once in 127 cases when ergonovine was administered intravenously at the end of the second stage; whereas the incidence increased appreciably in patients in whom the placental stage was left to natural forces and ergonovine was administered on its completion. The fact that the incidence of manual removal was once in 50 in the group which had received intravenous ergonovine at the end of the third stage can be explained on the basis that this procedure was carried out to reduce the hazard of post-partum hemorrhage. Furthermore, it will be noted that the blood loss was half as great where manual removal was necessitated following the use of ergonovine intravenously at the end of the second stage. Careful timing is important in the administration of ergonovine so that its effect can be exerted while the baby's body is still distending the uterine cavity. This procedure allows the baby to pass out of the upper segment, following which a powerful uterine contraction will shear off the placenta promptly. This is the most important factor in the prevention of incarceration of a completely or an incompletely separated placenta. The same uterine force properly timed will likewise expel the placenta from the uterus into the dilated uterine segment and vagina. Its prompt expulsion from this locality should follow.

DISCUSSION

The use of ergonovine intravenously as the baby emerges from the birth canal involves no new mechanism for placental separation and expulsion, but it perfects the normal mechanism. The powerful oxytocic drug administered when the baby is still distending the uterine cavity assures uterine contraction of maximum intensity as the baby leaves the birth canal. Such complete uterine action produces ideal physical conditions for prompt and complete placental separation. As the placental site suddenly shrinks away from the non-contractile placenta, the latter is cleanly sheared off its attachment. The same uterine contraction pushes the completely separated placenta from the contractile zone into the distended lower uterine segment and vagina. The marked uterine tonicity which is induced by ergonovine guards against further blood loss following placental separation. The drug likewise will maintain a state of tonicity for several hours, thereby preventing delayed post-partum bleeding.

The success of this third stage mechanism depends to a great degree on an accurate timing of the several events which comprise this period. Poor timing may result in the separation of the placenta, but it may be trapped in the contracted portion of the uterus. More rarely, a partially separated placenta may be incarcerated within the uterus. These accidents need not result in an excessive blood loss. After a short time the uterus may relax and the placenta can be easily expressed. In rare instances, manual removal of the placenta may be indicated. In spite of the fact that the drug has been in use during the past three and a half years by a host of physicians in training, these accidents occurred very

infrequently. The freedom from serious hemorrhage and complications in the third stage has been the most striking observation in this entire study. During the past two years the conduct of the third stage of labor just described has become routine on the House Service at the Chicago Lying-in Hospital.

CONCLUSIONS

A new method of conducting the placental stage of labor is described. Ergonovine is administered intravenously after the fetal head has been delivered and when easy egress of the shoulders has been assured. This results in an instantaneous separation of the placenta and its expulsion into the distended lower uterine segment and vagina. This procedure is applicable only to hospital practice. The marked reduction in blood loss and the very low incidence of complications in the third stage should result in a marked decrease in post-partum hemorrhage and its undesirable sequelae. Detailed observations are recorded in 2,006 patients, more than one-half of whom were treated by this new procedure.

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DISCUSSION

DR. W. C. DANFORTH.—Ergonovine is a valuable addition to our list of obstetric resources. I have had no experience with it in the third stage of labor, but we have for a long time used it routinely by intramuscular administration immediately after the delivery of the placenta. Blood loss has been diminished and uterovaginal tamponade for bleeding has become notably less in frequency.

The saving of blood at the time of delivery is important. Few clinics are accurately aware of the amount of blood which is lost for, without some form of measuring device, exact knowledge is impossible. It is certain that many estimates are inaccurate.

The mechanism of placental separation is better understood today than it used to be. The action of the contracting uterine muscle in severing the attachment of the noncontractile placenta is well brought out in the paper. Interference with this mechanism by early massage is properly criticized. Too early attempts to express the placenta often disturb the progress of separation and hinder rather than help.

If the process of separation and expulsion can be shortened without disturbing normal mechanism it is worth while. If normal mechanism is altered one cannot approve. In some of the radical suggestions for terminating the second stage or for initiating labor the normal series of events is changed. This must invite morbidity if not mortality.

The careful observations of the essayists seem to show that, although the process of delivering the placenta is hastened, the mechanism is not changed. That separation of the placenta must be complete before any attempt at expulsion is made is an obstetric law, the validity of which is recognized by the essayist.

That the use of an oxytocic in the third stage will reduce the time required for separation seems to be shown by our own experience with pituitrin, for the length of the third stage has decreased from fifteen to twenty minutes to about seven. The time, however, is a matter of secondary interest. The amount of blood loss is far more important. The tables indicate that the amount of blood lost has been materially decreased. If 81 per cent of more than 1,000 patients lost not more than 100 c.c. and only 4 per cent lost more than 200 c.c., the suggestion of the essayists commends itself seriously to us.

The old teaching, that ergot should never be given to an undelivered woman, with the single exception of abruptio placentae, was good. The prohibition of interference with the placental stage was also sound. Nonetheless, with the very greatly increased efficiency of the new alkaloidal preparation a change may be permitted. All forms of management should give way when demonstrably better ones appear.

DR. ROBERT M. GRIER.—In the past year at the Evanston Hospital, we delivered 1,004 mothers. Only 12 of these women had sufficient bleeding to warrant calling the condition a post-partum hemorrhage. Thirteen women had their uteri packed. Formerly hemorrhage was copious enough to require packing of the uterus about 35 times a year. Since we have been using ergonovine intravenously where serious bleeding appeared, this number has been reduced to one-third.

The response to ergonovine given intravenously can be felt within thirty seconds while one holds the uterus. We do not, however, inject ergonovine routinely at the end of the second stage as has been recommended by the essayist. We have employed it intravenously at the end of the third stage only when it was felt necessary, but give it intramuscularly routinely at that time.

DR. LOUIS RUDOLPH.—The essayists have indicated four cases in which the blood loss was 400 c.c. or more. I would like to inquire, why do we sometimes get hemorrhage in spite of the use of ergonovine? It is well known also that a severe post-partum hemorrhage may occur with a flaccid or fairly well-contracted uterus in which hysterectomy is necessary to save life.

Duncan and others have indicated that the maternal sinuses of the placental site are first closed by the contraction phase of the muscle tissue of the placental site. The contracted state of the maternal sinuses of the placental site is maintained by the specific property of brachystasis of the upper uterine segment of the parturient uterus. Dr. Davis has clearly shown that the uterine response to ergonovine is due to the property of muscle contractility, but it does not imply that brachystasis (retraction) has taken place.

The combined properties of contraction and brachystasis (retraction) lead to decreased and tortuous lumina of the maternal sinuses, stasis, and thrombosis, and these when maintained lead to organization. On the other hand, if the uterus responds only to the contraction phase, relaxation will follow and hemorrhage will occur from the maternal sinuses, on account of the absence of the essential property of brachystasis.

We do not know what controls brachystasis, but it is a specific property of the upper uterine segment of the parturient uterus. All oxytocics will cause increased contractility, but we do not know that they play any part in bringing about brachystasis. Ergonovine increases contractility, and with a normal degree of brachystasis of the uterine musculature it decreases the hemorrhage from the maternal sinuses. It is, however, no guarantee against post-partum hemorrhage.

DR. FRED L. ADAIR.—I would like to call attention to a point in the normal mechanism of separation of the placenta which is not exactly in accordance with what takes place when any stimulation of the uterus occurs following the adminis-

tration of ergonovine. When the uterus contracts after delivery, the portion of the uterine wall which is not covered with placenta becomes somewhat thickened while the uterine wall which underlies the placenta does not. As the normal process proceeds a gradual separation of the placenta occurs, as this portion of the uterine muscular wall contracts, thus completing the first phase of the third stage.

When ergonovine is administered just after the child's head is delivered, the whole uterus contracts, including that portion underlying the placenta, and so the first phase of the third stage is virtually completed before the child is expelled. By the time the child is outside the uterus the separated placenta lies in the uterine cavity. In other words, in the normal mechanism when the child is expelled there is still an uncontracted portion of the uterine wall at the placental site, whereas with the administration of ergonovine the first phase of the third stage is practically completed when the child is delivered.

With the increased number of operative deliveries, it is quite important that the subsequent procedures, such as repair, not be delayed. If you wait fifteen to thirty minutes for the normal expulsion of the placenta, it means that the patient has either to come out of the anesthetic or the anesthesia is continued for a longer period of time, both of which are more or less undesirable. This plan of treatment means that we can proceed more promptly with the post-partum care immediately following delivery of the placenta. Further, we have the very important fact that with a minimal loss of blood we resort less frequently to vaginal and uterine tamponade in order to clear the field for the repair of lacerations or repair of laparotomy wounds. Tamponade carries the danger of the introduction of infection.

DR. JOSEPH L. BAER.—We at Michael Reese Hospital likewise lend our approval to this procedure. However, the use of an oxytocic which is so potent requires more emphasis on the dangers than the essayist gave it. He spoke properly of the accurate timing of administration of this drug, and he mentioned that the shoulders should be impinged under the symphysis. This procedure is now to be published with the approval of a very considerable group, an authoritative group, including those who have discussed this paper. I can imagine the possibility of rupture of the uterus due to the violence of its contraction against the impacted shoulders, the head being completely delivered but the shoulders not having come through the inlet. Hence I think when this article goes into print there should be very decided emphasis placed on the specific risks that are inherent in this procedure. There is a place for this oxytocic if it is used according to the directions given and with foreknowledge of the potential dangers.

Finally, I would like to have Dr. Davis tell us their method of measurement of blood loss, because these measurements were given rather accurately in 100 c.c. units.

DR. DAVIS (closing).—We hesitated for a period of about three years before presenting this new management of the placental stage to the profession. In the interim, our method has been carefully investigated and approved in several other institutions. It was our impression, as Dr. Baer so well brought out, that if doctors found they could deliver the placenta in a fraction of a minute, or within a minute or two, that they would resort to the use of intravenous ergonovine indiscriminately. We felt that widespread use of this procedure could possibly result in serious consequences. We are convinced that the discriminate and intelligent use of the procedure described is safe.

I was interested in Dr. Grier's comment concerning uterine tamponade. I should like to tell you our experience in this regard. Prior to 1938 at the Chicago Lying-in Hospital we packed the uterus of about three women each month. In going over our statistics I found that uterine tamponade was carried out in 1 per cent of our deliveries, or 30 to 35 patients a year. During the last two years we resorted

to this procedure in a total of three instances. In two of these patients the tamponade was necessitated because of trauma. In all instances where intravenous ergonovine fails and the patient continues to bleed, a careful investigation of the reproductive tract should be made to rule out trauma as a cause of the bleeding. We have reduced the incidence of complications of the third stage tremendously since we have instituted the plan which we described.

One other thing I should like to point out is the use of ergonovine in breech delivery. We have been interested for many years in the use of an oxytocic drug in such cases. However, by the time the aftercoming head has left the uterine cavity and has reached the level of the perineum, the favorable mechanism for ergonovine intravenously has been lost. The drug should exert its influence when the uterine cavity is still distended with the baby's body. Obviously, in breech delivery this is not sound. In breech delivery ergonovine should not be administered intravenously until the placenta has been delivered. It can be given safely intramuscularly immediately after the baby is delivered so that its action will be delayed until placental separation and expulsion from the upper segment has been accomplished.

The method of estimating blood loss provides for considerable error. All the blood escaping from the vagina from the time the infant was delivered until the placenta was expressed was carefully collected by placing a basin at the buttocks. This basin was removed when there was no more bleeding from the uterine cavity and vagina. Obviously, some blood from the episiotomy was included in the measured loss. Our figures, therefore, represent more than the loss associated with placental separation and its delivery. Many women lose so little blood that the amount is difficult to measure, providing a bloodless placental stage.

Cobb, D. B.: Posterior Vaginal Hernia, South. M. J. 34: 196, 1941.

A ten-year review of the literature revealed only 42 reports dealing with this condition, and to these the author adds three of his own. The anatomic basis for posterior vaginal hernia is the weakness of the pelvic sling at the bottom of the pouch of Douglas where there is very little muscle tissue and scant fascial support. Excessive depth of the cul-de-sac may be a predisposing factor. The sac, which develops as elongation from the bottom of the pouch of Douglas, dissects between the layers of the rectovaginal septum and bulges beneath the posterior vaginal wall to emerge in the perineum; thus, it is a variety of perineal hernia. There may or may not be an associated general relaxation of pelvic structures.

There are no symptoms that are characteristically associated with this condition. The diagnosis, though easy to establish, is frequently missed because the lesion is not considered as a diagnostic possibility, and it is confused with the more common simple rectocele. Both may, however, co-exist. The hernia appears when the patient strains, and recedes when the recumbent position is assumed. When the examining finger in the rectum is pressed forward, the bulge of the posterior vaginal wall does not account for the entire vaginal mass, and the hernial sac can be seen and felt. Of significance is "the return of posterior vaginal protrusion after one or more operations for the relief of supposed rectocele."

The principles underlying cure of the condition are isolation and obliteration of the sac with repair of the defect. The condition of the pelvic floor and the presence of any associated genital abnormalities will influence the choice of procedure. Operation may be vaginal, abdominal, or combined abdominoperineal.

ARNOLD GOLDBERGER.

CLINICAL AND PHYSIOLOGIC ASPECTS OF UTERINE MOTILITY DURING PREGNANCY AND LABOR*

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THE analysis of uterine motility, here presented, is based upon the clinical study and recorded surface displacements secured with the capacigraph and mechanical ink writing recorder described in previous articles in this JOURNAL.[1,2] The use of equipment which can be used in a routine manner in the study of the motor activity of the uterus has one great advantage; namely, the accumulation of sufficient data to allow for statistical analysis. Thus, the collection of data becomes of minor importance; whereas, the analysis of the massed data becomes of major importance. Five hundred and two patients were studied and represent routine sampling of hospital admissions over a period of twelve months, during which about 3,000 patients were admitted. Over 5,000 large and over 5,000 small tracings of uterine contractions were available for analysis.

In this series there were 248 primiparas and 254 multiparas. Thirty cases were excluded from the series in the present study (19 multiparas and 11 primiparas) due to the employment of pituitrin or its derivatives. In view of the subsequent statistical analysis the classification as given in Table I is of considerable importance.

From the tabulated data, it is apparent that 89 multiparas and 93 primiparas were without pathology or medication. There are 144 primiparas and 146 multiparas who received medication or had some form of pathology or pathologic labor. One hundred and twenty-four of these received medication. Twenty-seven were mechanically induced while the remainder were distributed as shown in Table I. Furthermore, 47 of the primiparas and 64 of the multiparas were admitted with prematurely ruptured membranes, the majority having no pain on admission. The remainder had early, usual, or delayed rupture of the membranes.

In order to analyze our results statistically and to present a guide for future investigations, based upon the use of equipment measuring uterine displacements, the following classifications and standards were adopted.

TABLE I

	MULTIPARAS	PRIMIPARAS
No pathology, no medication	89	93
Sedation (morphine, scopolamine, phenolbarbital, dilaudid)	15	55
Progesterone	4	5
Castor oil and quinine	38	17
Pre-eclampsia	23	18
Mechanical induction	16	11
Section	19	10
Essential hypertension	14	5
Breech	2	11
Placenta previa	1	1
Abruptio placentae	2	1
Fibroids of uterus	1	3
Rupture of uterus	1	1
Arcuate uterus		1
Toxemia	5	2
Twins	3	
Hyperemesis		2
Renal disease	2	1

Any single contractural response was classified as large, small, or compound. Fig. 1 illustrates what is meant by a large single contraction, Fig. 2 a small single contraction, and Figs. 3 and 4 the compound contractions. The actual displacement of the abdominal wall in centimeters was obtained by dividing the recorded displacement by the amplification factor of the recorder. Measurements of recorded displacements are made from the abscissae to the summits of the curves. The over-all duration in seconds of the curve from beginning to end was ascertained. The onset was measured from the point whence the curves first left the abscissae, and from the end where the curve returned to the abscissae. The duration of the contractural phase (ascent) was measured from the onset to the summit and the relaxation phase (descent) from the summit to the termination of the curve. The over-all duration of the compound contractions was determined as in single curves, while the durations of the contraction and relaxation phases were ascertained by selecting the highest summit present in the curve and using that point as indicative of the end of contraction and onset of relaxation.

Since a complete recording represents a series of recurrent single contractions, the complete recordings were classified as consisting of intermittent large, small, mixed large and small, or compound contractions. Fig. 1 is an example of 3 recurring large contractions, Fig. 2 an example of 5 recurring small contractions, while Figs. 3 and 4 are examples of mixed large and small contractions. Intermittent recurrence of curves shown in Figs. 3 and 4 would be an illustration of sequential compound contractions. The complete recordings were analyzed in terms of frequency of (large, small, large and small, compound) contractions per hour. This was readily accomplished by noting the interval of time consumed by a fixed number of contractions, thence
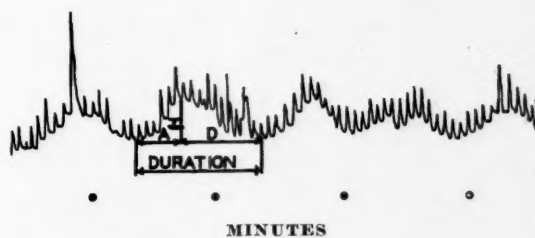
MINUTES
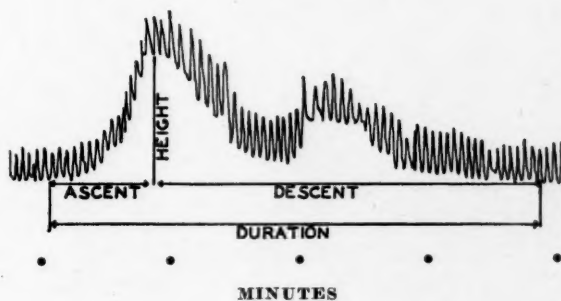
Fig. 1.

MINUTES

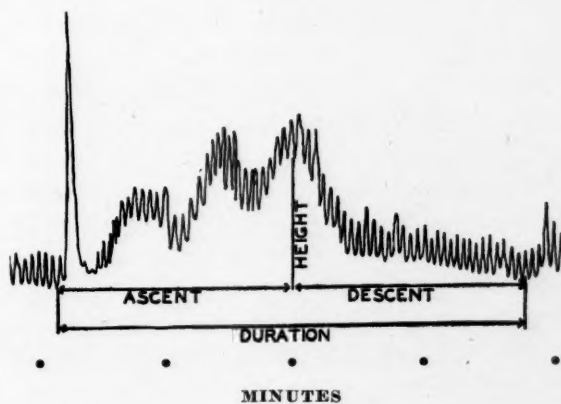Fig. 2.

MINUTES

Fig. 3.

MINUTES
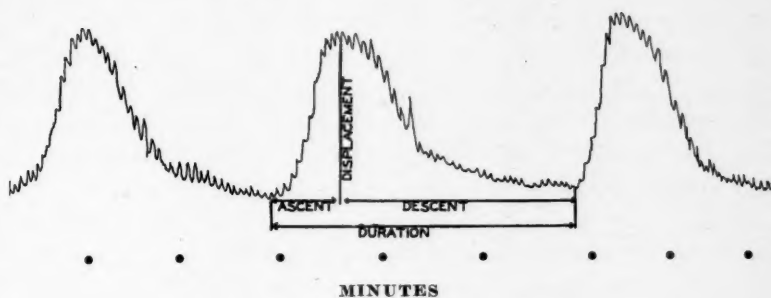
Fig. 4.

by mathematical calculation determine the theoretical number of contractions which would occur per hour.

The actual displacements in centimeters of all large unselected contractions present in all recordings and secured from all the patients studied were subjected to statistical analysis. The following formulas were used throughout in the statistical analysis.

$$\text{Arithmetical Mean } \widetilde{x} = \frac{\Sigma\,(f \times M.P.)}{N}$$

$$\text{Standard Deviation } \sigma = c\,\sqrt{\frac{\Sigma\,f\,(d')^2}{N} - \left(\frac{\Sigma\,f\,d'}{N}\right)^2}$$

$$\text{Standard Error } \overset{\sigma}{x} = \frac{\sigma}{\sqrt{N}}$$

$$\text{Significance Ratio} = \frac{\widetilde{x} - \widetilde{y}}{\sqrt{\left(\overset{\sigma}{x}\right)^2 + \left(\overset{\sigma}{y}\right)^2}}$$

Histograms constructed of the tabulated frequency distributions of the collected data show extremes of displacements varying from 0.1 cm. to 3.75 cm. For the most part these extremes represent the range of the recording equipment having an amplification of 4 to 1, rather than the true extremes known to occur from observations in which 0.1 mm. displacements were recognized with an amplification of 40 to 1. On the other hand with a 1 to 1 ratio, displacements of approximately 6.25 cm. have been recorded. From the grouped data, the arithmetical mean for the actual abdominal displacements secured from the combined recordings for multiparas and primiparas was 0.98 cm. The standard deviation was found to be 0.53 cm.

In order to determine possible basic differences in actual displacements in the records secured from unselected multiparas as compared to unselected primiparas, the large displacements of each class were treated separately and in a similar manner. Statistical comparison was then made with a resultant finding of a significance ratio of 2.45. A probability thus exists that the average displacement is larger in multiparas when treated as a class, than in a similar number of unselected primiparas.

The over-all durations of all large contractions were investigated. The arithmetical mean was found to be 154.8 seconds with a standard deviation of 60.28 seconds. Comparing the findings obtained from multiparas with those obtained from primiparas shows that a significant difference exists between the two classes. The average duration of the contractions of multiparas in the series were longer than the contractions of the primiparas.

The contraction phase and relaxation phase durations of the curves were analyzed to ascertain if the previously noted differences persisted.

The arithmetical mean for the contraction phases of all curves was 66.9 seconds with a standard deviation of 31.7 seconds. There exists a probable statistical difference between the primiparas and the multiparas. The contraction phase in multiparas is longer than the same phase in primiparas. The relaxation phase for all curves shows a mean of 88.4 seconds and a standard deviation of 43.6 seconds. The relaxation phase of the curves secured from multiparas tend to be longer in duration than similar phases secured from primiparas.

The arithmetic means and standard deviations found for the combined unselected multiparas and primiparas, unselected multiparas, and unselected primiparas are found in Table II (A, B, G). This table shows that the arithmetical means and standard deviations for displacements, over-all duration of contractions, duration of the contraction phase and relaxation phase are larger for the unselected multiparas than for the unselected primiparas. The respective significance ratios obtained by statistical comparison are shown in Table III (K). The significance ratios indicate that the differences are real and not due to chance.

In order to gain additional insight relative to the factors concerned in producing the observed large standard deviations and ascertain what would perhaps represent the "normal," the analysis was carried out on what is designated as "selected" cases. By a process of exclusion, all cases of sedation, premature rupture of membranes, twins, placenta previa, etc., were eliminated. The recordings used were obtained from those cases listed under "No medication, No pathology" and conforming to the following standards: Duration of pregnancy: 38 to 42 weeks; membranes ruptured at the usual time; duration of clinical labor: primiparas, twenty hours or less, multiparas, fifteen hours or less. Recordings limited to those obtained from primiparas zero to twenty hours before delivery, multiparas zero to fifteen hours before delivery.

The arithmetical means and standard deviations obtained from the recordings secured from "selected" primiparas and "selected" multiparas, gravida ii to xviii were compared with those obtained from unselected primiparas and unselected multiparas. The comparison of unselected primiparas and selected primiparas. Table II (G versus H) shows a definite improvement in the standard deviation for the duration of the contraction phase, relaxation phase, and over-all duration of the contractions. At the same time there was a reduction in the arithmetical means of the respective responses. Inspection of the frequency distribution curves of tabulated data shows greater symmetry than similar curves obtained from the unselected primiparas. The significance ratios obtained by statistical comparison are shown in Table III (G).

The comparison of the unselected multiparas and selected multiparas, gravida ii to xviii (Table II, B versus C) discloses improvement in the

TABLE II. ARITHMETIC MEANS AND STANDARD DEVIATIONS

	CONTRACTION PHASE		RELAXATION PHASE		OVER-ALL DURATION		DISPLACEMENT		FREQUENCY PER HOUR	
	X	σ	X	σ	X	σ	X	σ	X	σ
(A) Combined unselected multiparas and primiparas	66.38	32.33	88.48	43.64	154.86	60.28	0.98	0.54	17.5	8.96
(B) Unselected multiparas. Gr. ii to xviii	67.80	3203	91.19	46.90	158.99	63.07	1.03	0.57	16.3	8.70
(C) Selected multiparas. Gr. ii to xviii	69.57	28.42	91.67	50.12	161.24	69.04				
(D) Selected multiparas. Gr. ii to vi	65.45	23.90	86.37	42.39	151.82	51.64				
(E) Unselected multiparas with premature ruptured membranes. Gr. ii to xviii	64.42	28.13	82.24	39.70	146.66	54.81				
(F) Select multiparas with premature ruptured membranes. Gr. ii to vi	64.86	28.16	83.60	40.96	148.46	54.51				
(G) Unselected primiparas	64.96	31.80	86.76	37.90	151.72	55.78	0.96	0.50	18.5	8.90
(H) Selected primiparas	60.09	25.71	80.16	31.31	140.25	47.56				
(I) Unselected primiparas with premature ruptured membranes	68.72	37.58	84.02	41.32	152.74	59.21				
(J) Selected primiparas with premature ruptured membranes	67.29	41.44	84.75	32.83	152.04	46.80				

TABLE III

		SIGNIFICANCE RATIOS			
	DISPLACEMENT	CONTRACTION PHASE	RELAXATION PHASE	OVER-ALL DURATION	FREQUENCY
(A) Combined unselected multiparas and unselected primiparas versus unselected multiparas, Gr. ii to xviii	0.65	2.07	1.80	3.16	1.58
(B) Unselected multiparas, Gr. ii to xviii versus select multiparas, Gr. ii to xviii		1.17	0.19	0.25	
(C) Unselected multiparas, Gr. ii to xviii versus select multiparas, Gr. ii to vi		1.65	1.96	5.13	
(D) Unselected multiparas, Gr. ii to xviii versus unselected multiparas with premature rupture of membranes		2.87	3.75	4.87	
(E) Select multiparas, Gr. ii to vi versus select multiparas with premature rupture of membranes		0.29	0.89	1.03	
(F) Combined unselected multiparas and unselected primiparas versus unselected primiparas	0.97	1.49	2.48	3.16	1.42
(G) Unselected primiparas versus select primiparas		2.87	3.87	3.03	
(H) Unselected primiparas versus unselected primiparas with premature rupture of membranes		2.82	1.46	4.00	
(I) Selected primiparas versus selected primiparas with premature rupture of membranes		3.49	1.48	0.75	
(J) Selected primiparas with premature rupture of membranes versus selected multiparas with premature rupture of membranes		1.22	0.35	0.86	
(K) Unselected multiparas versus unselected primiparas	2.45	3.01	3.66	5.89	2.61
(L) Select multiparas, Gr. ii to vi versus select primiparas		2.65	2.10	0.65	
(M) Select multiparas with premature rupture of membranes, Gr. ii to vi versus select primiparas with premature rupture of membranes		1.22	0.35	0.86	

select group relative to the contraction phase, no improvement in the relaxation phase or the over-all duration; in fact, the standard deviation from the mean is increased with case selection.

Difficulty was initially experienced in accounting for these results. Investigation disclosed that many of the extremes found in the tabulated data for the selected multiparas were associated with multiparas. gravida vi to xviii. It was deemed advisable to exclude the findings of these cases from the class of selected multiparas. Analysis of the selected multiparas, gravida ii to vi, gave the following results (Table II, B versus D). Improvements in the standard deviations are present in the selected cases in regard to the contraction, relaxation phases and the over-all duration of the contractions. At the same time there occurs a general decrease in the arithmetical means. Inspection of the respective significance ratios (Table III, C) shows a significant decrease in the over-all duration while a possibility exists that the decrease in contraction and relaxation phases may exist. In general, the findings show tendencies similar to those observed in the primiparas.

The results obtained from the selected primiparas were compared with those obtained from the selected multiparas, gravida ii to vi (Table II, H versus D and Table III, L). The means for the contraction phase, relaxation phase and over-all duration are larger for the multiparas. The standard deviation for the relaxation phase and over-all duration are less for the primiparas than for the multiparas. No significant difference exists between the means of the over-all duration of contractions, but there exists a possibility that a significant difference exists between the relaxation phases and a probability that a statistically significant difference exists in the contraction phases.

In view of the number of primiparas and multiparas with prematurely ruptured membranes, it was deemed advisable to study these cases separately to determine their deviation from the "normal." In addition all the cases were analyzed in terms of duration of labor, time of rupture of the membranes compared to time of delivery, and duration of time between rupture of membranes and the onset of clinical labor. The following represent the means of each group.

Primiparas with early, usual or delayed rupture of membranes:

Clinical labor duration	17.0 hours
Rupture of membranes	4.3 hours before delivery
Interval between onset of labor and rupture of membranes	12.0 hours

Primiparas with premature rupture of membranes:

Clinical labor duration	16.6 hours
Rupture of membranes	23.6 hours before delivery
Interval between rupture of membranes and onset of labor	7.4 hours

Multiparas with early, usual or delayed rupture of membranes:

Clinical labor duration	11.5 hours
Rupture of membranes	3.4 hours before delivery
Interval between onset of labor and rupture of membranes	7.9 hours

Multiparas with premature rupture of membranes:

Clinical labor duration	6.6 hours
Rupture of membranes	27.4 hours before delivery
Interval between rupture of membranes and onset of labor	20.8 hours

From the above, the average duration of clinical labor for all primiparas was 16 plus hours; for all multiparas 9 plus hours. In the multiparas and primiparas with usual, early or delayed rupture of membranes, the average times for rupture of membranes before delivery were comparable (4.3 hr. and 3.4 hr.) with a mean of 3.85 hours. In the multiparas and primiparas with spontaneous premature rupture of membranes, the average times for rupture of membranes before delivery were comparable (23.6 hr. and 27.4 hr.) with a mean of 25.5 hours for the two classes. In primiparas with prematurely ruptured membranes, the average duration of clinical labor was 16.6 hours, a value comparing favorably with the average of seventeen hours for primiparas with unruptured membranes. In multiparas with spontaneous premature rupture of the membranes, the average duration of clinical labor was 6.6 hours which is considerably less than the average duration of clinical labor for multiparas (11.5 hours) with intact membranes. For primiparas, the average interval of latency between spontaneous rupture of membranes and the onset of clinical labor was 7.4 hours; whereas for multiparas it was 20.8 hours. This difference can be accounted for by the fact that there were in the multipara series 16 patients who were not at term and one of which had a latency of 356 hours. When the multiparas were limited to those patients of thirty-eight to forty-two weeks' pregnancy, the latency was found to be 12.5 hours. While those multiparas between twenty-eight and thirty-seven weeks of pregnancy had an average latency of 38.6 hours.

The contractions of multiparas with spontaneous premature rupture of membranes were analyzed separately in respect to the contraction, relaxation phases, and the over-all duration of the contractions. Findings in terms of arithmetical means and standard deviations are shown in Table II (E). Table III (D) shows the statistical ratios found when comparisons were made between the findings of the unselected multiparas with intact membranes and the unselected multiparas with ruptured membranes. The means of the contraction phase and relaxation phase and durations are larger for the multiparas with ruptured membranes, significantly so for duration and relaxation phase, and probably so for the contraction phase. On the other hand the findings in regard to the arithmetical means and standard deviations for selected multiparas (gravida ii to vi, with premature rupture of membranes) (Table II, F), do not differ significantly when compared to findings of the selected multiparas with unruptured membranes (Table III, E).

The contractions of the primiparas with spontaneous premature rupture of membranes were analyzed separately in respect to the con-

traction, relaxation phases, and over-all duration of the contractions. The results in terms of arithmetical means and standard deviations are shown in Table II (I). The statistical comparison of this class with corresponding unselected cases is shown by the ratios found in Table III (H). It is seen that the means of the over-all durations are increased, and on closer inspection the contraction phase plays the more prominent role in the increase. When the primiparas were selected according to the standards set up, the findings in terms of the mean and standard deviations are shown in Table II (J). These findings when statistically compared with selected primiparas (Table II, H), show the statistical ratios found in Table III (I). A significant difference exists only in the duration of the contraction phase. The selected primiparas with premature rupture of membranes when compared with selected multiparas with premature rupture of the membranes show no difference of statistical significance (Table III, J).

The duration of the contraction phase was statistically compared with the duration of the relaxation phase throughout all classes or groups of patients. Table II indicates that without exception the duration of the relaxation phases is significantly longer than the duration of the contraction phase. Table IV of significant ratios indicates that the chances are exceedingly remote that in any similar series of cases that the reverse would be true.

The over-all duration of the unselected small contractions secured from all sources were subjected to statistical analysis. The arithmetical mean was found to be 59.3 seconds and the standard deviation was 17.9 seconds.

Analysis was made of all the recordings in terms of frequency of large contractions per hour. Table II (A, B, and G) show the arithmetical means and standard deviations. The average frequency of large

TABLE IV

	SIGNIFICANCE RATIOS ASCENT VS DESCENT
Combine unselected multiparas and unselected primiparas	9.68
Unselected multiparas gravida ii to xviii	21.12
Selected multiparas gravida ii to xviii	8.00
Selected multiparas gravida ii to vi	8.02
Unselected multiparas with premature rupture of membranes	10.20
Selected multiparas with premature rupture of membranes	7.32
Unselected primiparas	20.66
Selected primiparas	8.24
Unselected primiparas with premature rupture of membranes	6.67
Selected primiparas with premature rupture of membranes	6.22

contractions was 17.5 per hour. No statistically significant difference in this connection was found to exist between the primiparas as a group and the multiparas as a group (Table III, A, F, and K).

Furthermore all recordings were analyzed in respect to the plus or minus percentage of spontaneous change in frequency response. In

selected patients in which individual recordings used were obtained fifteen hours or less before delivery and compared with those secured one or less hours before or after any individual recording, the mean plus or minus spontaneous change was found to be 27 per cent with a standard deviation of 15 per cent.

DISCUSSION

The recorders used in this investigation measure surface displacements; it is readily understood that topographic changes of the anterior abdominal wall are recorded. Our analysis shows that the displacements associated with uterine contractions are the result of the single or combined action of three uterine factors:

1. The change which occurs in the cross-sectional outline of the uterus with the rise in internal tension. This change is characteristic in that a fluid-filled organ having an ovoid cross-sectional outline becomes more spherical with a rise in internal tension. It has been ascertained with small to moderate resting intrauterine tensions that the displacement is large when compared to the acting tension and varies in a manner proportionate to the tension. With high resting internal tension, the displacement resulting from an increase of tension is small in comparison to the acting tension and not proportionately related to tension changes. With extremely high resting intrauterine tension, such as occurs in abruptio placentae, the displacements are very small.

2. The displacement component present and associated with uterine contractions in which there is either a localized or generalized thickening of the uterine wall.

3. The displacement produced by the resultant of acting forces tending to pull the organ anteriorly.

From our study it was apparent that displacements associated with uterine activity may be symmetric or asymmetric, localized or generalized, rhythmic, or arrhythmic, of the same intensity or of variable intensity, and at the same time, the tone level as reflected in the abscissae may remain constant or fluctuate above and below the arbitrary selected base line. The recordings obtained with the recorders used show changes in rhythm, intensity, and tone level. On the other hand asymmetric, symmetric, localized, or generalized uterine activities are indicated by notations placed on the recordings at the time of their observance.

We have found it necessary to distinguish between large and small contractions. The large are conventionally known as the Braxton Hicks of prelabor and are usually characterized by the generalized and coordinated nature in which the uterine muscle contracts. They are of relative long duration, and of relative great magnitude. These contractions have attributes similar to the prodromal or early intermittent contractions of labor and ultimately manifest themselves as true labor con-

tractions associated with the intermittent pains of labor. There is evidence of bilateral sources of excitation in which symmetrical halves of the uterus may be under the influence of separate excitation centers, this accounting for some asymmetric responses. Notations made on the recordings indicate that each half of the uterus responded asynchronously.

Theoretically, normal excitation and symmetrical action may involve either synchronous excitation from two sides, or asynchronous excitation in which the excitation developing from one side precedes that of the other side, or the excitation may involve but one side only.

The small contractions are of particular interest and are found present during pregnancy and labor. These contractions are characterized when present by their rhythm, relatively low amplitude and short duration. Singly or in combination with the large contractions they are apparently concerned in producing the changes known to take place in the lower uterine segment, previous to and during labor. Hence, they may be considered as evidence of preparatory uterine activity.

MINUTES
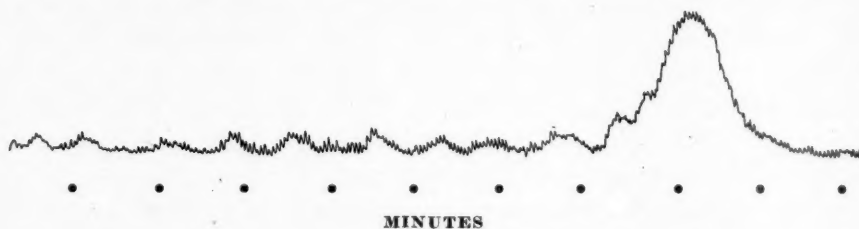
Fig. 5.

This activity may thus account for the placental separation in marginal or central placenta previa with the associated painless bleeding. Furthermore, the small contractions may be of such intensity during prodromal labor to call subjective attention to their presence as back pain, usually continuous but associated with exacerbations, having a frequency comparable to the frequency of the small contractions.

It is believed that the small contractions are derived from localized activity of the fundal musculature. Rhythmical excitation of limited range may account for their presence. There is evidence that such excitation may spread in a progressive manner to adjacent muscle until the whole of the uterine muscle is involved in a generalized coordinated response (Fig. 5). Caution must be exercised in identifying the small contractions. It is necessary to exclude the periodic fetal rolling movements and periodic variations in the amplitude of maternal respiration, particularly the variations occurring in the inspiratory phase of respiration.

That the large and small contractions may differ fundamentally one from the other may be surmised in view of the responses obtained with

oxytocic agents. The initial response in some instances is related to the excitation of those factors operating to produce the small contractions.

With reference to the statistical analysis, the evident tendency for larger uterine displacements in multiparas is primarily due to the general larger uterine size. The apparent difference in the over-all duration of the contractions in the two classes is due in part to a difference in the duration of the contraction and relaxation phases. There may exist fundamental differences in the manner of excitation, conduction, and response of the uterine muscle of the multiparas as compared to the primiparas. On the other hand, it is believed that selection of normal primiparas and normal multiparas, gravida ii to iv, of the same uterine size, same relative states of labor will show no significant differences in the temporal relationships of the individual contractions or phases.

The improvements in the findings which occurred with the elimination of pathologic and abnormal cases and the utilization of findings limited to those conforming to the standards set up is of interest. Apparently the excluded cases were the source of motility components, serving to modify the findings of the "normal." There exists a possibility that the excluded cases may be characterized by their specific abnormal motility.

The persistence of large standard deviations for the "normals" is in part indicative of the prevalence of compound and complex contractions. These contractions are evidences of incomplete or abnormal coordination of uterine muscle activity. They are present in patients having normal labor activity and are especially prevalent in early labor.

The increased durations of the contractions following rupture of the membranes is explained by a significant increase in the contraction phase. This is in line with the general clinical facts that with the loss of fluid, the intensity of the pains increase and the duration of the pains increase. The factor of ruptured members, apparently operates to modify the character and course of uterine motility during labor. Furthermore, we are of the opinion that spontaneous premature rupture of the membranes is not the cause of labor but the result of prodromal labor activity. This statement is qualified to the extent that it applies only to those patients at term and who have not been subjected to physical violence. Furthermore, in these patients the duration of clinical labor is the same, or less on the average than the duration of labor in patients with intact membranes.

There is a great deal of difference in respect to the time of admission and onset of clinical labor. Patients are urged to come to the hospital immediately upon notice of loss of fluid or blood per vaginam, irrespective of the presence or absence of pains. In these patients the time of admittance cannot be regarded as the onset of clinical labor, nor can the time of rupture of the membranes be considered as the onset of clin-

ical labor. Recordings were made on several patients resting in bed in whom the membranes ruptured spontaneously. The contractions recorded were not associated with pain and in fact the contractions were of insufficient strength to cause rupture of normal membranes.

The treatment of patients with spontaneous premature rupture of membranes should be correlated with motility studies. In view of the findings, it is not advisable as a routine procedure to stimulate with oxytocics the uteri of term patients with ruptured membranes, since danger of over activity may result in rupture of the uterus. The use of mild oxytocics is indicated when there is no progressive improvement of motility of recognizable quality twenty-four hours after the supposed rupture of the membranes. The absence of progressive improvement of motility suggests either unruptured membranes or an abnormal motility state.

The specific findings obtained by statistical analysis serve to provide standards for comparisons. The findings from any single or series of cases may be compared with those obtained from a large series of cases. One application is illustrated in the following manner: The uterus of a term multipara was stimulated with galvanic current using bipolar leads. As a result of this procedure, there was a pronounced change in the type of motility which persisted for thirty minutes. During this period there occurred four contractions having the following means: Contraction phase, 360 seconds; relaxation phase, 51 seconds; over-all duration, 411 seconds. Applying methods of statistical analysis, it is possible to predict that 99.7 times out of a hundred the observation in respect to the contraction phase and over-all duration were significant and not due to chance.

SUMMARY

1. A standardized method for making temporal analysis of uterine displacement curves is presented.

2. Additional evidence in respect to two fundamentally important uterine displacement components, namely, the large and the small, is presented.

3. Accumulated findings have been subjected to statistical analysis in which the displacement in centimeters, the duration in seconds of contraction phase and relaxation phase, and over-all duration were investigated in unselected and selected cases. Arithmetical means and standard deviations were determined and significance ratios ascertained by use of the standard error.

4. The application of the findings for assay purposes is illustrated in the text.

CONCLUSIONS

1. The displacements tend to be larger in the unselected multiparas than in the unselected primiparas, due in part to the difference in the size of the uterus.

2. The unselected multiparas as a class have longer contractions than the unselected primiparas as a class, due to combined increase in contraction and relaxation phases.

3. The data from selected cases have frequency distribution curves, showing less skewness and more symmetry than unselected cases. Selected cases provide means and standard deviations which represent the normal according to the standards established for analysis. Unusual and pathologic cases may possess specific abnormal motility. Selected multiparas and selected primiparas, standardized with one another, will show no significant difference in the temporal relationships of the large contractions.

4. Under standard conditions a spontaneous plus or minus 27 per cent change in the frequency of large contractions represents the average expectations.

5. Anterior displacement of the abdominal wall during an uterine contraction can be explained by purely physical means, change in cross-sectional outline, thickening of the uterine wall, and action of forces pulling the uterus forward.

6. Large and small contractions, independent or dependent upon one another, serve a useful function in preparing the lower uterine segment for labor.

7. Labor motility is inaugurated in advance of the development of labor pains.

I wish to express my gratitude to Drs. F. L. Adair and M. E. Davis for their helpful cooperation, timely advice, and suggestions during the course of this study.

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Londres, G.: Incidence of Syphilis in a Hospital and Private Clinic, Rev. méd. munic. (Rio de Janeiro) 1: 167, 1941.

The author reports a remarkably high incidence of syphilis in an unselected group of 500 women and 1,000 men in his clinics (Rio de Janeiro). It is noted, however, that most of the patients are in a roughly selected class as they all have cardiovascular complaints. Of 500 women, 137 (31.4 per cent) were found to be syphilitic by clinical, serologic and in some instances post-mortem findings. Of 1,000 men, 470 (47 per cent) were syphilitic.

A group of 349 cases was divided as follows: secondary syphilis 17, tertiary syphilis 185, central nervous system syphilis 9, latent syphilis 111, and heredosyphilis 27.

The author concludes that the popularization and employment of individual methods of protection should be the basis of the attack on the problem of syphilis.

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WOUND DISRUPTION AND ITS MANAGEMENT*

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THE high mortality which attends the disruption of abdominal wounds makes this postoperative complication vitally important. Fortunately, it is of relatively infrequent incidence but, nevertheless, may at times contribute quite noticeably to the list of preventable fatalities. Any procedure, which may be of material value in reducing postoperative mortality, is deserving of serious consideration. It is for this reason that our study of wound disruption and its management is presented.

From 1933 to 1940, there were never over one or two eviscerations on our service of 1,300 laparotomies a year, so that very little attention was directed to this infrequent complication. However, when six occurred in 1940 with a mortality of 50 per cent, an investigation and analytic study were made. Considerable interest was aroused when it was found that the three deaths were in patients who were in good condition at the time of evisceration, were repaired layer by layer, and died of peritonitis. The two patients repaired by simple through-and-through suture of all layers lived. Believing this relationship of type of repair to mortality to be more than coincidental, we decided to study all the cases of wound disruption occurring on the gynecological service from January, 1933, to July, 1941, a period of eight and one-half years. Records beyond this period would not permit a careful study and accurate analysis of the individual cases. We were particularly interested in finding the most common causes of wound disruption. But above all, we wanted to determine how important the type of secondary closure was in affecting the mortality rate.

Brettauer,[1] in 1899, was the first to describe this condition in the American literature with a report of three cases. Larger series have since then been reported by Madelung,[2] Sokolov,[3] Meleney and Howes,[4] Glenn and Moore,[5] and Fallis.[6] The collective review of 1,458 cases of disruption by Hartzell and Winfield,[7] in 1939, gives an excellent summary of the literature. One is impressed with the variety of statistics and opinions as to etiology and management of this complication. This, in itself, indicates that the contributing factors are many and the management is not a universally accepted routine.

Absolute prevention of this complication is impossible, as mentioned by Downs.[8] For, notwithstanding the many articles written in the past decade regarding the importance of suture materials and the methods of applying them, there still remains a definite incidence of wound disruption.   Therefore, a concerted effort should be made to minimize the incidence and cautiously manage those cases which must inevitably occur. That the incidence can be lowered is clearly demonstrated by Glenn and Moore[5] who discovered important etiologic factors in their first study which they believe have improved the results in the second report.

A review of the 10,725 laparotomies done on the gynecologic service during the past eight and one-half years revealed 16 eviscerations or total abdominal wound disruptions (Table I).   The incidence of 0.15 per cent is comparatively low (average reported 1.83 per cent).   Noteworthy are the 11 deaths in these 16 cases, revealing a high mortality of 68.7 per cent (average reported 34.8 per cent).   The day of disruption varied from the second postoperative to the twelfth, average being the seventh (Table II).

TABLE I.   INCIDENCE OF DISRUPTIONS

Total number of laparotomies (Exclusive of McBurney's incisions)	10,725
Number of total disruptions	16
Incidence of disruption	15 per cent
Number of deaths following disruption	11
Mortality in disruptions	68.7 per cent

TABLE II.   CONTRIBUTING FACTORS

FACTOR	FREQUENCY
Severe coughing	9 cases
Severe emesis	9 cases
Abdominal distention	8 cases
No tension sutures	6 cases
Infected wound	8 cases
Drain through wound	2 cases
Obese wall	2 cases
Malignancy	0 cases

The most common factors associated with these 16 cases of disruption were: cough, 9 cases; emesis, 9 cases; distention, 8 cases; no tension sutures, 6 cases; infected wounds, 8 cases; drain, 2 cases; obese wall, 2 cases; and malignancy, 0 cases (Table II).

The type of secondary closure in these 16 cases was as follows: 7 closed layer-by-layer, 7 by simple through-and-through suture including all layers, 1 by tampon and adhesive bridges, and 1 patient died before any treatment could be instituted.   Of the 7 cases closed layer-by-layer, 6 patients died, all of peritonitis.   Of the 7 closed by simple through-and-through suture only 3 died, 1 due to peritonitis (pelvic abscess was present at time of repair), 1 due to bronchopneumonia, and 1 due to a pulmonary embolus.   The only patient treated with tampon and bridges died on the day of evisceration due to cardiac failure (Table III).

TABLE III. DAY OF DISRUPTIONS

CASE AGE	DIAGNOSIS	OPERATION	PRIMARY CLOSURE*	DAY DIS-RUPTION†
1. M. B. 33	Fibroid uterus Ventral hernia	Supracervical hysterectomy Repair of hernia	ccg no tensions	PO IX
2. C. S. 49	Fibroid Chronic salpingitis	Supracervical hysterectomy Salpingo-oophorectomy	ccg swg tensions	PO VI
3. E. N. 39	Chronic pelvic inflammatory disease and cysto-urethrocele	Laparotomy Vaginal plastic	ccg swg tensions	PO VI
4. A. K. 50	Fibroid Diabetes	Supracervical hysterectomy Salpingo-oophorectomy	ccg no tensions	PO VII
5. L. K. 26	Pseudomucinous cyst of ovary	Supracervical hysterectomy Salpingo-oophorectomy	ccg swg tensions	PO V
6. E. B. 38	Fibroid	Supracervical hysterectomy Salpingo-oophorectomy	ccg swg tensions	PO VII
7. D. J. 45	Fibroid Chronic salpingitis	Supracervical hysterectomy Salpingo-oophorectomy	ccg swg tensions	PO IX
8. M. M. 38	Fibroid Chronic cervicitis	Total hysterectomy	ccg swg tensions	PO V
9. L. M. 53	Degenerated fibroid Cardiac	Total hysterectomy	ccg no tensions	PO XII
10. D. B. 41	Left ovarian cyst Adhesions	Left salpingo-oophorectomy	ccg no tensions	PO III
11. A. K. 56	Fibroid Chronic pelvic inflammatory disease	Supracervical hysterectomy	ccg swg tensions	PO IX
12. M. G. 34	Fibroid Chronic salpingitis	Supracervical hysterectomy	ccg swg tensions	PO II
13. M. J. 45	Fibroid Chronic salpingitis	Supracervical hysterectomy	ccg swg tensions	PO VIII
14. H. W. 38	Fibroid Chronic salpingitis	Supracervical hysterectomy Salpingo-oophorectomy	ccg no tensions	PO VII
15. M. R. 65	Fibroid Prolapse	Myomectomy and suspension Colporrhaphy	ccg drain no tensions	PO VII
16. M. J.	Fibroid Chronic salpingitis	Total hysterectomy Salpingo-oophorectomy	ccg drain no tensions	PO XII

*ccg, chromic catgut; swg, silkworm gut.
†Po, postoperative.

It is interesting to note that Bettman and Lichtenstein[9] in their review of 7,500 laparotomies at Michael Reese did not think that coughing, emesis, infection, and omission of tension sutures were of great etiologic importance. However, the summary by Hartzell and Winfield[7] indicated that conditions which increase the intra-abdominal pressure are contributing factors in wound disruption. Reading through these charts, especially noting the interns' and nurses' progress notes, in a majority of these cases the evisceration seemed imminent a day or so before it occurred.

Only two of the patients had drains (12½ per cent), but this is a relatively high percentage since very few laparotomies are drained through

TABLE IV. CAUSE OF DEATH

CASE	CONDITION AT TIME OF DISRUPTION	SECONDARY CLOSURE	ANESTHETIC	RESULT*	CAUSE OF DEATH
1. M. B.	Fair	Layers	Ether	Died PE III	Peritonitis
2. C. S.	Poor	Layers	Ether	Died PE I	Peritonitis
3. E. N.	Terminal	No repair	0	Died immediately	Peritonitis and bronchopneumonia
4. A. K.	Fair	Through-and-through braided silk	Ether	Died PE I	Bronchopneumonia
5. L. K.	Good	Through-and-through braided silk	Ether	Home PE XX	----
6. E. B.	Poor (abscess)	Through-and-through braided silk	Nitrous oxide	Died PE VIII	Peritonitis
7. D. J.	Good	Through-and-through braided silk	Ether	Died PE III	Pulmonary embolus
8. M. M.	Good	Layers	Nitrous oxide	Died PE XVII	Peritonitis
9. L. M.	Poor cardiac	Tampon and bridge	0	Died PEO	Cardiac failure
10 D. B.	Poor	Layers	Ether	Home PE XI	----
11. A. K.	Good	Layers	Cyclopropane	Died PE V	Peritonitis
12. M.G.	Good	Layers	Spinal	Died PE III	Peritonitis
13. M. J.	Good	Through-and-through silk-worm gut	Cyclopropane	Home PE XVII	----
14. H. W.	Poor	Through-and-through silver wire	Spinal	Home PE 60	----
15. M. R.	Good	Layers	I. V. Pentothal	Died PE VI	Peritonitis
16. M. J.	Poor	Through-and-through braided silk	I. V. Pentothal	Home PE XVIII	----

*PE, Postevisceration.

the wound on our service. When we consider the logical explanation of wound dehiscence by Freeman[10] as being due to an omental wedge forcing its way through an incompletely closed peritoneum, obviously a drain invites such a process, the actual rupture being precipitated by sudden coughing, sneezing, or emesis.

Most authors have reported a definite incidence of malignancy among these cases (average 22 per cent) which suggests this condition as a likely contributing factor. However, we found no cases of malignancy in this group of complete disruptions. This seems more unusual when one considers the large number of laparotomies for malignant cases on our service. Many patients with Group III and IV carcinoma of the cervix

have had laparotomies for internal iliac artery ligation and for pelvic sympathectomy. These patients would seem very poor risks, owing to the far-advanced carcinoma and previous extensive radiation. Yet only one patient had a *partial* evisceration on the tenth day (Greenhill and Schmitz[11]).

Much has been written about the importance of vitamin C in wound healing. Wolfer[12] demonstrated low cevitamic acid levels in patients at the time of evisceration. On our service on this basis, one would expect many wounds not to heal. It must be remembered that our patients are nearly all poor negroes and whites, most often in a state of avitaminosis. Also, we do not give cevitamic acid to these patients routinely either pre- or postoperatively. Just the occasional case with a noticeable avitaminosis receives vitamin therapy. The same can be said of hypoproteinemia; even though it has been shown to be a contributing factor by the work of Thompson, Ravdin, and Frank.[13]

The type of suture material has been stressed as an important factor.

Whipple and Elliott[14] advise the use of silk in abdominal closure. Spool cotton throughout is advocated by Meade and Ochsner.[15] Closure of the abdomen by through-and-through silver wire sutures in all cases, where there is likely to be infection or excessive strain, has been used successfully by Reid, Zinninger, and Merrell.[16] Babcock[17] reports the allergic reaction of tissues to chromic catgut as a cause of wound disruption. Norris[18] points out the loss of tensile strength with iodized catgut, due to an increased perishability rate because of the destructive action of iodine on the catgut.

However, our methods have been rather contradictory to the above teachings. Because we have eight different services in our department of gynecology, eight different methods are used to close the abdomen. All of the surgeons use iodized catgut, but in addition some use fine silk, heavy silk, silver wire, and silkworm gut. All abdomens are closed in layers, i.e., peritoneum, transversalis fascia, rectus fascia, subcutaneous layer (if thick), and skin. About two-thirds of the operators use tension sutures and one-third do not. Also interesting is the fact that most of these abdomens have been closed by interns, after a few demonstrations.

A consideration of all these seemingly contradictory reports brings up the question as to what is the cause of wound disruption. Obviously, disruption is due to a disturbance in wound healing.

According to Mason[19] the process of healing may be divided into three phases, i.e., (1) *Exudative* or lag period, lasting four to five days during which the strength of tissue union is low. (2) *Fibroblastic* stage, from the fifth to the sixteenth day when the wound attains the maximum strength afforded by a connective tissue scar. (3) *Stage of maturation* or differentiation for fascia, tendon, and bone.

Keeping this fundamental process in mind, it is logical to believe that any one of many factors may be responsible for the disruption. These factors may be classified for convenience as follows:

A. *General Conditions:*
    1. Type of patient, obese, asthenic
    2. Malnutrition, hypoproteinemia
    3. Avitaminosis, low ascorbic acid level
    4. Dehydration
    5. Malignancy, especially if previous radiation has been given
    6. Presence of acute or chronic pelvic inflammation

B. *Local Conditions:*
    1. Method of primary closure, failure to make careful anatomic layer-by-layer closure
    2. Type of suture, strength and lasting ability insufficient
    3. Size and quantity of suture, too heavy and too much
    4. Interference with blood supply of tissues, too tightly sutured
    5. Irritants such as strong antiseptics and *drains*
    6. Presence of hemorrhage and blood clots in wound
    7. Infection in wound
    8. Failure to provide rest and immobilization of wound until fibroplasia is well established (twelve to fourteen days)

C. *Unexpected Postoperative Complications:*
    1. Abdominal distention
    2. Severe coughing
    3. Persistent emesis
    4. Hiccoughing
    5. Sitting up or getting up too soon.

Such a list of indirect causes would explain why the number of good reports of the past decade seem contradictory. A consideration of this list also explains why there will always be eviscerations and why a good method of management is essential.

An evisceration is a true surgical emergency and gives one the same sort of uneasy feeling as to observe an eclamptic convulsion.

A good description of this complication by Shipley[20] is as follows: "The edges of the wound are usually necrotic, the different layers are more or less sealed together with the exposed intestine dull in color and often covered by exudate—one hates to be called to see them."

It is the type of complication which makes the surgeon feel embarrassed, as though his technique were faulty. But in our series, all the operators in the department had this complication, and there was no preponderance of incidence on any one service. The treatment must be carefully decided according to the best interests of the individual case.

When evisceration occurs, the first consideration is whether the patient's condition is satisfactory to withstand a secondary closure. If there is already a generalized peritonitis, pelvic abscess, severe cardiac

pathology, or pneumonia, this patient is best treated with sterile gauze tampon and firm adhesive strapping. Several days later, when the patient is improved, a satisfactory secondary closure may be done.

If secondary closure is to be done at the time of evisceration, the patient is given ¼ gr. of morphine, strapped with adhesive, advised against coughing or straining, and taken to the operating room. The type of anesthesia is very important, especially since many of these patients have been coughing for several days before this accident. General anesthesia is to be avoided if at all possible. One of the patients in our series died of a bronchopneumonia which was attributed to the ether anesthesia for secondary repair. Now intravenous or spinal anesthesia is preferred. Local infiltration has been used, but infiltration of an infected area is unsatisfactory and dangerous.

The surgical preparation is quite simple. Since the tissues exposed are all potentially infected, we just clean the surrounding skin with normal saline and alcohol, avoiding any excessive manipulation of the exposed bowel. We do not believe strong antiseptics or meticulous cleansing procedures are indicated or worth while in this instance.

A nonabsorbable type of suture is used which may be a No. 12 braided silk, silver wire, or silkworm gut. No attempt is made to separate and identify the layers of the abdominal wall, as this would mean considerable manipulation of an infected area. Besides, this is unnecessary for good closure and adds to the possibility of peritonitis which is the most common cause of death following evisceration. With a large cutting-needle on each end, the suture is brought through the entire wall from within the peritoneal cavity to the skin surface, two inches from the edges. These sutures are not tied but held taut until all have been placed (1½ inches apart). This makes the insertion of the last few easier; also the tying is an important procedure for good apposition. As the operator draws these through-and-through sutures up for tying, the assistant keeps his hand inside the peritoneal cavity for two reasons; first, to make sure that the peritoneum is closely approximated, and second, to prevent a loop of bowel from being caught in the closure.

Now the postoperative care becomes more important than ever: adequate fluids to combat dehydration, 3,000 to 4,000 c.c. a day, a high protein diet, and 300 mg. of cevitamic acid daily. All coughing must be prevented by sufficient sedation; a Wangensteen suction for upper abdominal distention or vomiting and a Miller-Abbott tube for small bowel obstruction. Chemotherapy in the form of 100 c.c. of 5 per cent sodium sulfathiazole may be given intravenously as needed for peritonitis. The sutures are left in place until healing is complete; this may take three weeks. The patient is then allowed up. These patients must be examined carefully in six weeks for a ventral hernia.

One may ask why we feel so certain that simple through-and-through secondary closure is the best method. There are two good reasons to

substantiate this thought. First, it is an accepted surgical principle that the least amount of trauma and manipulation in an infected field is to be preferred. To do a layer-by-layer repair one must dissect these layers apart, then puncture each layer many times with a needle and introduce a relatively large amount of suture to retard healing. Second, and most important, our analysis of the 16 cases in the past eight and one-half years bears this out. Of the seven cases closed in layers, 6 of the patients died of peritonitis and 4 of these were in good condition at the time evisceration occurred. Of the 7 cases closed by simple through-and-through suture, 3 patients died, but only one because of peritonitis; this patient had a pelvic abscess at the time of evisceration. The other two deaths were due to pulmonary embolus and bronchopneumonia following a general anesthetic.

A careful study of the wound disruptions on another surgical ward during this same period of eight and one-half years was made. In 1,366 laparotomies, there were 6 eviscerations, an incidence of 0.44 per cent (ours 0.15 per cent) which corresponds with Hesseltine's[21] report from the Chicago Lying-in Hospital. There was one death, a mortality rate of 16.6 per cent (ours 68.7 per cent). However, a more interesting fact is that only one case was repaired in layers and this was the patient that died of peritonitis. The 5 patients that recovered had a simple through-and-through closure. One of these cases which eviscerated twice is of interest. The patient was treated conservatively by tampon and bridging until her condition improved, when a satisfactory closure could be made. She recovered.

A careful analysis of the case histories in this group of wound disruptions has been interesting and very educational for us. One becomes evisceration-conscious in his work after such a study. It has often been said that good postoperative care means the treatment of complications before they arise. The incidence of wound disruption can be lowered by keeping in mind the contributing factors as mentioned before. The high mortality of this complication can be reduced by this simple through-and-through type of secondary closure.

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DISCUSSION

DR. H. CLOSE HESSELTINE.—This paper covers the various conditions which have been charged with contributing to disruption of abdominal wounds. The method and management of the secondary closure are in accord with most of the recent reports, namely, closure with the least possible manipulation with non-absorbable suture material, usually by mass suturing rather than individual tissue approximation, the appropriate treatment for complications, such as peritonitis and cough.

The incidence reported by Dr. Schmitz and Dr. Beaton is very much below that which has been given as the average. On the other hand, the mortality in their group is appreciably higher than the average. Perhaps the mortality rate does not result so much from the disruption as it does from the condition which may have been more or less responsible for the disruption, such as peritonitis.

Bohlender and I made a report in 1940 before this Society of our observations of this complication at the Chicago Lying-in Hospital. At that time, we reported 15 eviscerations in 3,179 abdominal operations, an incidence of 0.47 per cent. Since the compilation of those data, there have been 935 abdominal operations, both obstetric and gynecologic, without a single abdominal disruption. This apparent improvement seems to have resulted from exercise of greater care in the primary closure and by combating those conditions which may predispose to evisceration. Ordinarily, most of our patients are in good health and on a fairly well-balanced diet. Although sufficient determinations have not been made, it has been assumed that our patients are usually not deficient in vitamin C. We have made no attempt to administer ascorbic acid or to prescribe high protein diet pre- or postoperatively.

It does not seem justifiable to follow a routine for every patient, in accordance with recent suggestions, of a three- to four-day preparation with a high caloric diet, high protein, and high vitamin C and B. This should apply only to those actually in need of one or more of the factors.

DR. CHARLES E. GALLOWAY.—Probably the reason why such a large number of eviscerations is reported is that the interns in the County Hospital close the wounds. I am glad to hear this problem stressed, because otherwise there will be 15,000 eviscerations in the United States every year and about four or five thousand of the patients will die.

DR. SCHMITZ (closing).—Concerning closure of the wounds by interns, I would like to say that in this series the attending surgeons closed the peritoneum, and they, therefore, are probably responsible for the end results.

A STUDY OF CONTRACTIONS IN LABOR BASED ON KYMOGRAPHIC RECORDS OBTAINED FROM AN INTRAUTERINE BALLOON

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(From the Evangeline Booth Hospital)

MOST obstetricians will agree that the efficiency of uterine contractions is the single most important factor in the mechanism of labor. Failure of the uterus to contract normally and to relax adequately between contractions results in slow dilatation of the cervix, incomplete flexion of the fetal head, delay in normal rotation, and slow descent. Much emphasis has been placed in the past upon the maternal pelvis and its relation to cephalopelvic dystocia. Adequate diagnostic means are now available for the measurement and classification of the pelvic diameters, thus permitting the obstetrician to predict with fair accuracy any impending dystocia between the fetal head and the birth canal. Unfortunately, no precision instrument such as the x-ray is available for the study of uterine muscle physiology.

Factors influencing the contractions of uterine muscle fibers have received much attention in recent years, but still we do not know why the uterus contracts. That smooth muscle has the capacity for intrinsic motility is well known. There must be several factors, physical and chemical, which determine the nature of the contractions. A recent report on uterine motility[1] makes it clear that the hormones play an important part in the initiation of contractions and their pattern after they have been established. It has now been shown that both estrogen and progesterone fall off sharply a few days before the onset of labor. In the pregnant uterus at term, the hormones must play an important role, the nature of which is not understood. More important perhaps than the chemical factors may be those of a purely mechanical nature. It has been suggested that the onset of labor may result from distention, which puts the muscle fibers under tension; ischemia results and contractions follow.[2] The well-known fact that artificial rupture of the membranes at term will induce labor tends to invalidate the distention theory as the cause of labor.

The nature of these contractions has been studied by several investigators. The first of these to use an intrauterine balloon for recording contractions on a kymograph was Schatz[3] in 1872. Rucker,[4] in 1925, used the Voorhees bag and recorded the tracings of uterine contractions in labor. He demonstrated graphically for the first time the oxytocic ef-

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fect of posterior pituitary extract. Many reports have appeared since that time, most of them concerned with studies on excised muscle. Others have utilized a distended balloon in the cervix. As far as I know, this is the first report on uterine contractions studied by means of a distended balloon in the active, contractile portion of the fundus uteri with the membranes intact. This report will describe the normal uterine contractions of spontaneous labor at term and the effect of ruptured membranes on the pattern of uterine motility.

TECHNICAL PROCEDURE*

The observations recorded here were made upon young primiparas who were under my care at the Evangeline Booth Hospital in Richmond. Their cooperation was obtained without difficulty. In the 22 cases studied to date by the technique to be described, there has been no instance of intra-partum or post-partum complication resulting from the experimental procedure. In order to study the effect of ruptured membranes upon uterine contractions, it was necessary to select patients in whom the balloon could be passed extraovularly without injury to the membranes. By recording the contractions in such a case with intact membranes and then observing the change which occurred when the membranes rupture, a basis of comparison was established. Four cases who fulfilled these requirements have been selected from the total group and the tracings upon these comprise this report.

A small condom balloon was attached to a specially designed linen catheter, somewhat heavier than that used by the urologist for ureteral catheterization. The catheter was long enough to permit insertion of the balloon well up into the fundus and still permit its opposite end to protrude from the vagina. It was necessary to pass the balloon early in labor before the presenting part became fixed in the pelvis. With the aid of a uterine dressing forceps, it was possible to insert the balloon between the membranes and the uterine wall, leaving the amniotic sac undisturbed. The catheter was then connected by a rubber tube to the mechanical ink recorder. The system was filled with sterile water, the rubber tube and catheter having been previously sterilized, and sufficient water was introduced to raise the pressure to 80 mm. of mercury. The tracings of uterine contractions were then recorded on a revolving kymograph equipped with a timer. The catheter and balloon were allowed to remain in the uterus throughout labor and were expelled after delivery of the fetus.

CASE 1.—The first patient was permitted to go through labor without interference and the membranes ruptured spontaneously during the early part of the second stage. The first stage of labor was considered to end after full dilatation of the cervix, regardless of the state of the membranes. The first tracing was taken two hours after the onset of labor. Contractions occurred every five to seven minutes, were relatively low and somewhat variable in amplitude, and there was a moderate degree of tetany. This is the typical picture of early first-stage contractions (Fig. 1). As labor progresses to full dilatation of the

*The illustration of the instrument for this procedure was published in this JOURNAL 42: 1024, 1941.

cervix, there is a marked change in the pattern of uterine contractions. The second tracing on this case taken early in the second stage, thirty minutes after full dilatation, shows considerable increase in the degree of tetany. The contractions occur at more frequent intervals, every
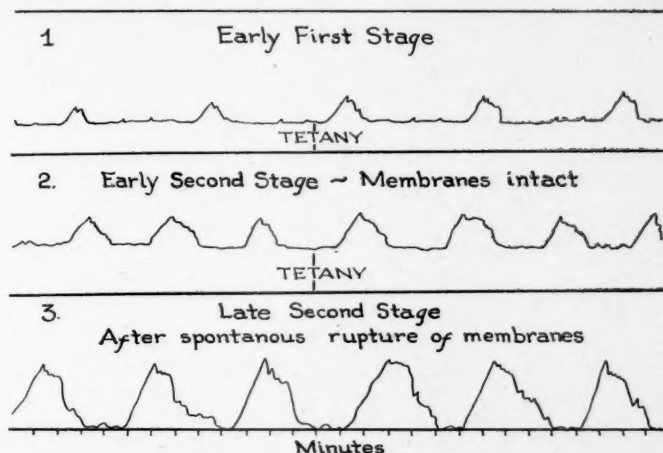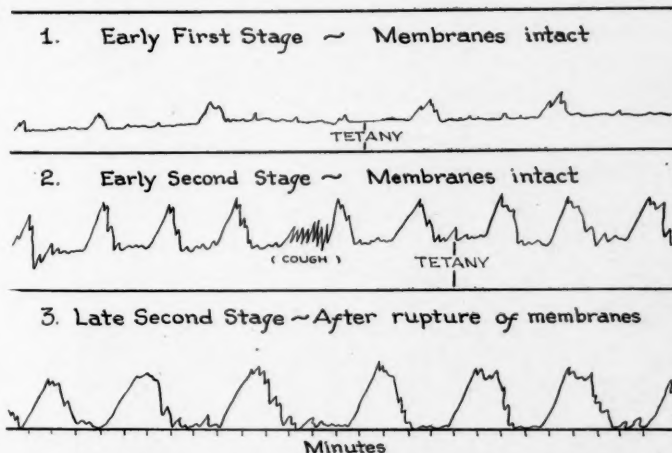

Fig. 1.—Case 1. After spontaneous rupture of the membranes, the uterus loses its tetany, relaxes between contractions, and each contraction becomes more efficient. Note in this and all other tracings that the duration of contractions may sometimes be as long as three minutes. Uterine contractions begin some time before they can be palpated or perceived by the patient. Actually the patient experiences pain during a relatively short interval in any contraction.

Fig. 2.—Case 2. After spontaneous rupture of the membranes in the second stage, the uterus loses its tetany, relaxes between contractions and the amplitude of each contraction increases.

three minutes, have a somewhat longer duration, but the actual excursion of each contraction is not increased because the tetany prevents full relaxation between contractions. The membranes ruptured spontaneously thirty minutes after the second tracing was taken. It will be observed now that tetany has been abolished; and as a result, the ampli-

tude of each contraction is increased. The relaxation of the uterus fol-
lowing spontaneous rupture of the membranes during the second stage
greatly increases the efficiency of each contraction (Fig. 1).
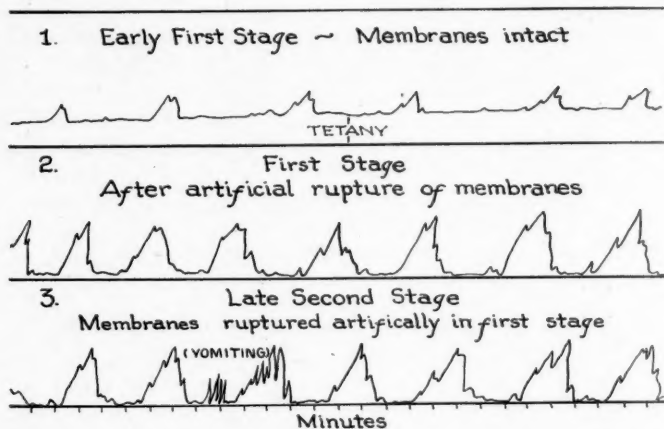
Fig. 3.—Case 3. After artificial rupture of the membranes during the first stage,
tetany is abolished and the contractions assume the high amplitude seen after spon-
taneous rupture.
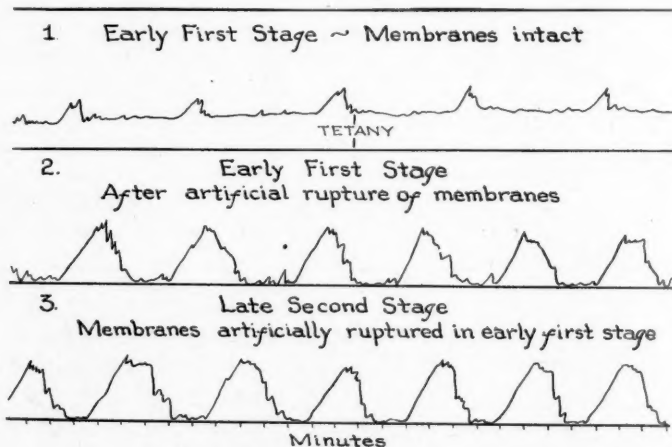
Fig. 4.—Case 4. After artificial rupture of the membranes during the first stage,
the uterus loses its tetany and the contractions increase in amplitude such as occurs
after spontaneous rupture during the second stage.

CASE 2.—The first tracing was taken on this patient three hours after
the onset of labor. These early first-stage contractions show a relatively
low, somewhat variable amplitude superimposed on a moderate degree
of tetany. During the early second stage and while the membranes were
still intact, it may be seen that the tetany has increased. The contrac-
tions became more painful, but in spite of this their expulsive efficiency
was not augmented because of the tetany. One hour and twenty min-
utes after this tracing the membranes ruptured spontaneously. The
tracing taken during the late second-stage showed the absence of tetany

with a much higher rise in each excursion of the writing point. It must follow that the efficiency of each contraction is thereby increased (Fig. 2).

CASE 3.—Early first-stage contractions recorded two hours after the onset of labor showed the irregular, low amplitude, mildly tetanic contractions characteristic of this stage of labor. In this case the membranes were ruptured artificially immediately after the first tracing was recorded. The second tracing taken one hour later and before the cervix was fully dilated reveals the absence of tetany. Even before the end of the first stage, the uterus relaxed between each contraction. The tracings assumed the high amplitude characteristic of second-stage contractions after spontaneous rupture of the membranes. The third tracing taken during the late second stage shows that the pattern of motility which follows rupture of the membranes persists throughout labor (Fig. 3).

CASE 4.—The early first-stage contractions are similar to those already described. Immediately after this tracing was taken the membranes were ruptured artificially. The second tracing taken thirty minutes later shows that tetany has been abolished and each contraction assumes the high amplitude characteristic of the uterus which relaxes adequately between pains. The third tracing taken during the late second stage shows that the pattern of motility produced by artificial rupture of the membranes persists throughout labor (Fig. 4).

CONCLUSIONS

1. The extraovular, high fundal, intrauterine balloon connected to a mechanical ink recorder has been used to study the patterns of uterine motility during labor.

2. Labor contractions during the early first stage have a relatively low amplitude superimposed on moderate tetany. As labor progresses with intact membranes tetany becomes more marked.

3. Labor contractions after rupture of the membranes, spontaneous or artificial, are characterized by the absence of tetany. The increased amplitude which results augments the expulsive efficiency of each contraction.

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807 WEST FRANKLIN STREET

AN ANALYSIS OF ABORTION DEATHS IN THE DISTRICT OF COLUMBIA FOR THE YEARS 1938, 1939, 1940

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IN THE cities where maternal mortality studies have been made, a noticeable reduction in the number of deaths has been reported. Physicians who have attended the meetings of such committees or have been members of the committees are all aware of the sobering effect of the verdict "death preventable—responsibility assigned to the physician because of lack of judgment." Accordingly, by these means the profession has succeeded in raising its own standards of maternal care to a considerable degree but has devised no effective control over the abortionist as yet.

The committee on maternal mortality of the District of Columbia has been functioning since June, 1937. It reports that 24 per cent of maternal deaths in the District are due to abortions.[4, 5] This finding has been consistent in studies made throughout the country, as is shown in the Children's Bureau Report for 1934 (p. 103),[2] and the earlier Philadelphia Obstetrical Board studies for the years 1931 and 1933.[3] Another way of stating the problem is that deaths following abortion constitute nearly half of all maternal deaths from septicemia,[2] and that in the District of Columbia report[4, 5] 36 per cent of all preventable maternal deaths from whatever cause and at whatever stage of pregnancy are due to abortion.

The following is an analysis of abortion deaths in the District occurring in the period from Jan. 1, 1938, through Dec. 31, 1940. The total maternal deaths under twenty weeks of gestation are presented in Table I. In 22 per cent of these cases, death is not due to abortion (Group A). It is reasonable to suppose that future reports will show a decreased incidence in deaths from these causes, since treatment for hyperemesis is improving and the attention of the profession is being drawn to the importance of the early diagnosis of ectopic pregnancy.

In Group B (5 cases, or 7 per cent of the total), death occurred in pregnant women who were suffering from a fatal intercurrent disease. These deaths are not primarily maternal deaths but deaths from various diseases where pregnancy is an associated condition, and the abortions in this group are perhaps the only ones which can be unequivocally labeled as spontaneous.

TABLE I. DEATHS UNDER 20 WEEKS' GESTATION IN DISTRICT OF COLUMBIA MATERNAL MORTALITY STUDY JANUARY, 1938, TO DECEMBER, 1940

		NUMBER	PER CENT
A. Deaths from various causes		17	22
Hyperemesis	3		
Hydatidiform mole	1		
Ectopic pregnancy	13		
B. Deaths following abortions associated with fatal intercurrent disease		5	7
Acute leucemia	1		
Pneumonia	2		
Pyelitis	1		
Rheumatic fever with congestive failure and post-abortal hemorrhage	1		
C. Deaths following abortions		54	71
1. No evidence of induction	10		
2. Induced abortion deaths	44		
Total		76	100

The remaining 54 cases (Group C) comprising 71 per cent of the total deaths occurring in pregnant women up to the twentieth week of gestation are abortion deaths.

Of these 54 cases there were 10, or 18.5 per cent, where we could find no evidence of induction in the medical record or in the autopsy report. A summary of these cases is given in Table II. However, neither could we prove that all ten were spontaneous.

TABLE II. GROUP C. DEATHS FOLLOWING ABORTIONS

		NUMBER	PER CENT
1. No evidence of induction		10	18.5
a. Abortion with degenerating fibroid	1		
b. Out-of-town cases with no history	2		
c. Patient moribund on admission	1		
d. Operative interference and/or numerous vaginal examinations	4		
e. Pregnancy denied	2		
2. Induced abortion deaths		44	81.5
Total		54	100.0

The following case (Group C 1 a), which came under our personal observation, tends to bear out Hamilton's contention that "the incomplete spontaneous abortion offers the same nidus as retained secundines post partum; the uterus recognizes no moral distinctions."[1]

Gallinger Municipal Hospital (No. B4246). B. S., aged 37, colored, married, gravida ii, para 0. History of menorrhagia and metrorrhagia of three months' duration. Admitted Oct. 20, 1939, for hysterectomy. Diagnosis: Fibromyoma uteri. Discharged Oct. 23, 1939, without operation on account of upper respiratory infection. Readmitted Nov. 3, 1939, with history of spontaneous incomplete abortion with bleeding since October 24. Dilatation and curettage on November 5. Septic course ending in death on November 11 in spite of chemotherapy and frequent transfusions.

Pathologic findings: Specimen from dilatation and curettage showed necrotic placenta. Post-mortem findings, 4 cm. necrotic foul-smelling fibroid. Intramural fibroid above internal os.

Diagnosis: Septicemia, acute gangrenous and suppurative myometritis.

Whereas the evidence favors the diagnosis of spontaneous abortion in this case, one cannot be as positive about the other nine.

Although no evidence of induction was found in the history or autopsy of these 9 cases, the records do not differ from those where induction was admitted in the history or was shown by the post-mortem examination.

Perhaps 4 women in this group died because of unwise operative procedures or neglected hemorrhage, but one cannot prove that interference with the pregnancy may not have been attempted first. Laparotomies and the shuttling of patients from one hospital to another occur in cases of admitted induction. Where no evidence of induction exists, the out-of-town patients with no history and those who deny pregnancy are most under suspicion. In the known induced group, the autopsy does not necessarily reveal a recently traumatized cervix in a multipara who has inserted a catheter and more than one woman who claims to have fallen accidentally turns out to have a ruptured uterus or a lacerated internal os at necropsy. Therefore we do not consider that we are going outside the limits of probability in suggesting that at least half of the cases where no evidence of induction was available were actually induced.

Among the 44 deaths (Group C 2) where evidence of induction exists, these constituted 81.5 per cent of the total abortion deaths (Group C), and if we add one-half of the cases from the group just described, we can say that 90 per cent of the abortion deaths in the District of Columbia in the past three years were due to induced abortions.

The major cause of abortion deaths (Table III) is what it has always been, sepsis. In only 3, or 5.6 per cent of the total abortion deaths, sepsis was not the major problem.

Among those who died of septicemia, 3 cases were associated with ectopic pregnancy. It is fair to ask whether the patient would have died in these cases had an induced abortion been attempted in the presence of an intrauterine pregnancy alone, but one may add that had an induced abortion not been attempted at all a diagnosis of ectopic pregnancy might have been more quickly made. Physicians must constantly bear in mind that neither the patient, herself, nor the abortionist are accomplished gynecologists and that more than one abortion is attempted in the presence of extrauterine pregnancy.

Another patient died following a mismatched transfusion, but had she not tried to abort herself she probably would not have needed the transfusion.

TABLE III. CAUSE OF DEATH IN 54 ABORTION CASES

		NUMBER	PER CENT
I. Sepsis		51	94.4
1. No evidence of induction available	10		
2. Induced abortions	41		
a. Sepsis alone	36		
b. Sepsis associated with ectopic pregnancy	3		
c. Sepsis associated with transfusion reaction	1		
d. Sepsis associated with possible poisoning	1		
II. Nonseptic Deaths		3	5.6
Air embolism	2		
Poison	1		
Total		54	100.0

The question sometimes arises as to whether the patient was pregnant at all at the time an abortion was attempted. We know definitely of one such case where no evidence of pregnancy was found by the hospital pathologist post mortem, and it is not accordingly listed as a maternal death. That there may actually be others among the 54 is a fair surmise, as a positive diagnosis of early pregnancy cannot always be made without a microscope, and the coroner's office of the District of Columbia does not give a microscopic report.

Air embolism was given as the cause of death in three pregnant women; only two are listed here, as in the third, pregnancy had progressed beyond the twentieth week. In all three cases the individual was found dead on the premises where abortion had been attempted. An inquest was made in one of these cases. Criminal proceedings followed. A registered nurse pleaded guilty and was sentenced to three years in the penitentiary. The criminal record mentions the use of a catheter but does not go into further details. No inquest was made in the other two cases; they were signed out as "self-induced" by the homicide squad.

This brings up the question of the preventability of these abortion deaths. According to the usual coding of Maternal Mortality Committees, abortion deaths are classified as preventable, the responsibility being assigned to the patient. Our analysis (Table IV) of the medical

TABLE IV. COMPARISON OF MEDICAL AND POLICE RECORDS

SOURCE	MEDICAL RECORD		HOMICIDE SQUAD RECORD	
	NUMBER	PER CENT	NUMBER	PER CENT
Self	17	39	28	64
Second party	12	27	4	9
Unknown	15	34	12	27
Total	44	100	44	100

record of the 44 known induced cases shows that 39 per cent were self-induced and 27 per cent were admittedly performed by a second party.

As far as the last 34 per cent are concerned, we have the post-mortem evidence of perforated uterus, or lacerated internal os, that these abortions were induced, but we do not know by whom, or when and how they were performed. A comparative analysis of the homicide squad records shows that of the total 44 cases, 29 cases, or 63 per cent, were signed out as self-induced abortions. Four persons were brought up before the Grand Jury and only one was convicted. Another conviction was made in the case of a woman where a six months' pregnancy was interrupted, resulting in the premature birth of an infant which lived six days. This case is not included in the total of 44 cases.

Such a record is not an unusual one and should not be taken to reflect discredit on the police or the Courts of the District of Columbia in particular but rather on the American scene in general. Convictions in cases of criminal abortion are few and far between.[6] Statutes are on the books of every State prescribing punishment for any person who induces an abortion. The law further prescribes that it is the duty of one who knows of a case of criminal abortion to report it to the police. Actually the records of the Narcotic Division of the District of Columbia to whom cases are supposed to be reported show that 79 cases of abortions were reported in the course of two and one-half years, obviously an infinitesimal fraction of the number of cases performed in the District.

During the period from June, 1938, to May, 1941, 12 individuals were brought before the Grand Jury; 7 of these were convicted and sentenced to from one to three years in the penitentiary. The occupations recorded for these abortionists include two physicians, one chiropractor, one registered nurse, four practical nurses, one post-office clerk, one auto mechanic, one forger, and one pharmacist. There were 2 colored and 10 white individuals.

TABLE V. POLICE RECORD, HOMICIDE SQUAD

SELF INDUCED	OUT OF TOWN	NATURAL	NOT KNOWN TO POLICE	TO GRAND JURY		TOTAL
				CONV.	EXON.	
28	7	2	3	1	3	44

The difference between the medical record and the police record (Table IV and Table V) in the assignment of the cause of death reflects the problem known to everyone who has been connected with a criminal abortion case. The abortionist's lawyers are experienced in the tactics of delay; witnesses for the prosecution back out at the last moment; the jury will not find the abortionist guilty for, as a member of the police force told the author, "on any jury you are sure to find that some juryman's wife has had an abortion performed at some time." In other words, everyone tries to dodge the issue and nothing happens. In one famous case, a physician, aged 65 years, was first arrested in 1929, being rearrested nine times before he was convicted in 1937. In

3 of these cases, the patient on whom he was accused of performing an illegal abortion died. Another doctor, aged 75 years, was found not guilty by the jury in a case involving the death of a young girl in 1939, and has three other indictments pending before the Grand Jury, one of them involving a death. At date of writing he was still out on bail.

SUMMARY AND CONCLUSIONS

1. Fifty-four women died from abortions in the District of Columbia in the period from January, 1938, to December, 1940. This constitutes 24 per cent of the total maternal mortality deaths, or 71 per cent of deaths in pregnant women before the twentieth week of gestation.

2. Ten, or 18.5 per cent, of these 54 cases showed no evidence of induction, but the cases could not be proved to be spontaneous. Death from uncomplicated spontaneous abortion is probably very rare.

3. Forty-four, or 81.4 per cent, of these cases were induced. Thirty-nine per cent were self-induced; in 27 per cent of the cases, the patient admitted outside interference; in the last 34 per cent post-mortem findings were the only evidence of induction.

4. Sepsis was the principal cause of death in all but three cases out of a total of 54.

5. In connection with four of these deaths, one abortionist was tried and found guilty, three others were exonerated.

6. During the period July, 1938, to May, 1941, twelve abortionists were brought before the Grand Jury in the District of Columbia. Seven were convicted. This sampling of abortionists includes two licensed physicians, one forger, one auto mechanic, and one post-office clerk.

The remedy does not lie entirely in a change of the law. The District abortion law is cited by Taussig[6] as one of the most liberal in the United States, since an abortion is permitted "when necessary to preserve the woman's life or *health* and under the direction of a licensed practitioner of medicine." This provision of the law seems to be taken advantage of only by the unscrupulous abortionist and can be used as an excuse by him in court. Reputable physicians perform abortions only where there is a clear-cut medical reason showing that the mother's life is endangered.

Ideally, of course, no abortion should be performed except in an open hospital under the most careful medical supervision.

Failing this, the following measures, tending to the simultaneous education and policing of the public and community, are suggested:

1. A public health educational campaign on the dangers of abortion, both criminal and self-induced.

2. Education of the public to seek medical treatment immediately following an induced abortion.

3. A concerted effort on the part of the public, the medical profession, the police, and courts to drive the most unskillful operators in a community out of business.

4. Acceptance of responsibility for the treatment of abortion patients by local hospitals instead of shunting these patients from one hospital to another.

5. Vigorous treatment of sepsis by chemotherapy and transfusion with a minimum of manipulation.

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WEIGHT STUDIES IN PREGNANCY

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WEIGHT studies during pregnancy are neither unimportant nor all-important. Primarily, weight determination establishes an indicant to the subject's dietary habits and exertive actions and as an augury in certain cases of impending toxemia. Other interpretations of its value are alluded to such as regulation of fetal weight gain, effect upon duration of labor, increase in complications, etc.

The present report, based upon observations in 3,230 women during pregnancy, parturition, and post partum, is rather to interpret factually the findings than to record a mass of data, and then to draw some conclusions on the worth of routine weight taking and the limitations circumscribing its practical applications.

DATA OBTAINED

The usual weight of the patient was taken as the base, unless there had been a sudden weight gain prior to pregnancy. The weight charts

began at the second to the sixth month of pregnancy and records were made at least at monthly intervals until delivery. In the majority and in all toxic patients, weighings were at one- to two-week intervals during the last six weeks of pregnancy. The weight was again noted four to six weeks post partum.

The character of the labor, its duration, the type of pelvis, and dystocia due to bony and soft parts were noted. Complicating factors, notably pregnancy toxemia, were recorded. The change in the patient's weight post partum with respect to her usual weight and pregnancy gain was indicated. The baby's birth weight was registered in each case.

ANALYSIS OF DATA

As will be seen from Tables I to VI-A, the weight charts were first arranged according to age groups, and averages for weight gain, fetal weight, and hours of labor computed for each five-year group from fifteen to forty-five years. This is detailed in Table I.

Table II records the fetal birth weight in mothers gaining from one to sixty pounds in five-pound groups, and Table II-A, those in mothers losing up to 10 pounds throughout a pregnancy.

The duration of labor ratio to pounds gained during pregnancy is recorded in Table III and to weight loss, in Table III-A.

Delivery analysis of weight gain groups is recorded in Table IV and Table IV-A. "Delivery other than normal" includes elective low forceps in these and the succeeding tables and consequent increased incidence is manifest.

TABLE I

3,230 cases		
Average increase in weight	23.2	pounds
Age group from 16 to 20 years	600	cases
a. Average weight increased	24.8	pounds
b. Average fetal weight	7.2	pounds
c. Average duration of labor	15	hours
Age group from 21 to 25 years	1,136	cases
a. Average weight increased	24.5	pounds
b. Average fetal weight	7.4	pounds
c. Average duration of labor	17	hours
Age group from 26 to 30 years	884	cases
a. Average weight increased	23.5	pounds
b. Average fetal weight	7.5	pounds
c. Average duration of labor	17	hours
Age group from 31 to 35 years	425	cases
a. Average weight increased	19.6	pounds
b. Average fetal weight	7.7	pounds
c. Average duration of labor	16.5	hours
Age group from 36 to 40 years	165	cases
a. Average weight increased	16.4	pounds
b. Average fetal weight	7.2	pounds
c. Average duration of labor	13	hours
Age group from 41 to 45 years	20	cases
a. Average weight increased	18	pounds
b. Average fetal weight	7.7	pounds
c. Average duration of labor	11	hours

TABLE II. FETAL WEIGHT RATIO TO WEIGHT GAINED DURING PREGNANCY

POUNDS GAINED	NUMBER OF CASES	FETAL WEIGHT
1- 5	51	7.2
6-10	149	7.4
11-15	446	7.3
16-20	648	7.5
21-25	623	7.4
26-30	507	7.3
31-35	329	7.6
36-40	235	7.6
41-45	98	7.8
46-50	42	8.1
51-55	12	7.5
56-60	10	10.5

TABLE II-A. FETAL WEIGHT RATIO TO WEIGHT LOST DURING PREGNANCY

POUNDS LOST	NUMBER OF CASES	FETAL WEIGHT
1- 5	53	7.6
6-10	27	7.4

TABLE III. DURATION OF LABOR RATIO TO POUNDS GAINED DURING PREGNANCY

WEIGHT GAIN	NUMBER OF CASES	DURATION OF LABOR (HOURS)
1- 5	51	13.5
6-10	149	12.3
11-15	446	14.6
16-20	648	16.0
21-25	623	17.0
26-30	507	17.6
31-35	329	15.5
36-40	235	15.8
41-45	98	17.2
46-50	42	18.8
51-55	12	17.2
56-60	10	28.0

TABLE III-A. DURATION OF LABOR RATIO TO POUNDS LOST DURING PREGNANCY

WEIGHT LOSS	NUMBER OF CASES	DURATION OF LABOR (HOURS)
1- 5	53	16.0
6-10	27	10.5

TABLE IV. DELIVERY ANALYSIS OF WEIGHT GAIN GROUPS

POUNDS GAINED	NUMBER CASES	NORMAL DELIVERY	DELIVERIES OTHER THAN NORMAL
1- 5	51	45—88.2%	6—11.8%
6-10	149	120—66.6%	29—33.3%
11-15	446	366—74.9%	80—24.9%
16-20	648	496—65.7%	152—33.6%
21-25	623	400—62.4%	223—36.8%
26-30	507	270—60.7%	237—39.2%
31-35	329	196—60.6%	133—39.3%
36-40	235	164—69.4%	71—30.3%
41-45	98	60—55.5%	38—44.4%
46-50	42	30—60.0%	12—40.0%
51-55	12	6—50.0%	6—50.0%
56-60	10	7—70.0%	3—30.0%

The delivery analysis of age groups is given in Table V.

Complications for groups gaining 1 to 60 pounds and losing 1 to 10 are recorded in Tables VI and VI-A.

The incidence of toxemia of pregnancy, mild to severe, including eclampsia, is recorded for the twenty-one to twenty-five age groups,

TABLE IV-A. DELIVERY ANALYSIS OF WEIGHT LOSS GROUPS

POUNDS LOST	NUMBER CASES	NORMAL DELIVERY	DELIVERIES OTHER THAN NORMAL
1- 5	53	47	6
6-10	27	25	2

TABLE V

GROUP	NORMAL DELIVERY	ABNORMAL DELIVERY
16-20	426—71%	174—28.0%
21-25	692—61%	444—39.0%
26-30	564—64%	320—36.0%
31-35	342—80%	83—20.0%
36-40	125—75%	40—24.3%
41-45	12—60%	8—40.0%

TABLE VI. COMPLICATIONS IN GROUPS GAINING

GROUP	NO. CASES	COMPLICATIONS	% COMPLICATIONS
1- 5	51	7	14.0
6-10	149	42	28.0
11-15	446	51	11.4
16-20	648	67	10.3
21-25	623	59	9.4
26-30	507	81	16.0
31-35	329	77	23.4
36-40	235	39	16.6
41-45	98	16	16.3
46-50	42	19	45.0
51-55	12	3	25.0
56-60	10	4	40.0

TABLE VI-A. COMPLICATIONS IN GROUPS LOSING

GROUP	NO. CASES	COMPLICATIONS
1- 5	53	8
6-10	27	4

TABLE VII. INCIDENCE OF TOXEMIA

AGE GROUP	NO. CASES	TOXEMIA CASES	% TOXEMIA
21-25	1,136	67	5.9

TABLE VII-A. INCIDENCE OF TOXEMIA

WEIGHT GROUP	NO. CASES	TOXEMIA CASES	% TOXEMIA
21-25	623	22	3.5
26-30	507	28	5.5
31-35	329	39	11.8
Total	1,459	89	Average 6.1

which is numerically the largest (Table VII). The table also gives the same data for weight groups 21-25, 26-30, and 31-35, which total a comparable number.

<div align="center">DISCUSSION</div>

Something definitive may be said from the data recorded in table form, but there also are some no less important observations not easily portrayable without being involved and confusing. The average weight gained in the 3,230 cases was 23.2 pounds, ranging in the five-year age groups from 16 to 45 from 16.4 to 24.8 pounds. It is of interest that the older groups gained less. It is also true that the average "usual weight" of the older groups was greater, indicating a tendency for those of normal or less than normal weight to gain proportionately more during pregnancy than those who were overweight. It is noted that the fetal weight is not influenced by maternal weight changes (barring one small group gaining 55 to 60 pounds during pregnancy). This is in accord with competent observations on "war babies" and impressions of many years. The average fetal weight for the entire series was 7.4 pounds.

Except for the extreme group of 55 to 60 pounds gain, the duration of labor may be said to be essentially uninfluenced by weight gain. There are notable exceptions to this rule, however, which "averages" do not cover. Patients gaining more than 25 pounds have nearly 10 per cent greater chance of operative delivery than those gaining less, and the hazards of anesthesia and perineal infection are considerably greater.

In the analysis by age groups, the incidence of normal delivery indicates a higher percentage of normal delivery in the older (and multiparous) age ranges. However, while the older age groups had higher *normal delivery* ratings, they also had higher percentages of complications, as also indicated in Table VI of the weight groups. But a young primipara of normal weight gain (23.2 pounds) is a better prospect than a multipara of any age who has gained excessively.

Since excessive weight gain is commonly believed to be associated with or conducive to toxemia of pregnancy, Tables VII and VII-A are of more than ordinary interest. Private observations of a large number of these patients likewise permits some latitude in the interpretation of the findings. The numerically largest age group (twenty-one to twenty-five) had a toxemia incidence of 5.9 per cent. In the weight groups of 21 to 25 pounds, the incidence was 3.5 per cent; 26 to 30 pounds, 5.5 per cent; while from 31 to 35 pounds it rose sharply to 11.8 per cent. Casual translation of these data might lead one to believe that weight gain per se was of vital importance in causing or preceding toxemia. A moderately capacious experience will recall many patients with toxemia of varying severity with no excessive (or even less than normal) weight

gains. And the vast majority of those who gain excessively do not become toxemic. The consequence of this is not negated by the data given in Table VII-A. Recollection of patients rather than figures recalls three more or less distinct groups gaining excessively; namely, those with considerable edema, mostly static; those "bloated" patients with minimal pitting edema but obvious increase in body fluids; and those whose weight gain is largely due to tissue gain. Thus some patients are obviously hydropic without having or developing toxemia, while others with "occult edema" either increasing interstitial fluid with no static accumulations or undergoing hygroplasmic changes in their protoplasm, are more likely subjects. A *sensation* of swollen hands or face thus assumes greater importance than pitting edema in patients gaining weight. And in the matter of evenness of weight gain those patients developing toxemia did not begin to gain rapidly until the characteristic loss of fluid balancing power shared by most toxemic patients had become evident. In other words, excessive fluid accumulation, generally but not always present in toxemic patients, is a concomitant factor in toxemia development, a symptom as it were of the complex itself. It suggests an increased incidence of toxemia, more especially in those patients with "occult edema" showing moderate upward fluctuations in blood pressure. And it is this group in the early stages who respond best to dehydration therapy.

Among those whose excessive weight gain is mostly stereoplasm it is our belief that toxemia incidence is not increased.

The post-partum weight loss is dependent upon the amount and type of weight gain, the hydropic gainers returning to or below their usual weight within two weeks of parturition, while the tissue gainers are likely to retain most of the weight gained in excess of the normal increment. Roughly, in the latter group it may be said that patients will retain beyond six weeks 60 to 80 per cent of all weight gained in excess of 22 pounds. In patients with either static or occult edema, no such calculation is permissible, inasmuch as the causative factors in the first and the control of fluid balance in the second produce a rapid water loss within a few days of delivery.

Since all of the patients were cautioned to limit weight gain in pregnancy to 20 to 25 pounds, a mild lowering of the general average weight has been effected.

The increment by trimesters is of some interest. There is generally little gain in the first three months, although glaring exceptions may be observed when a huge appetite substitutes for the more commonly observed nausea and vomiting of pregnancy. The majority fall into the following categories:

> First 3 months, 2 to 3 pounds gain
> Second 3 months, 8 pounds gain
> Third 3 months, 12 pounds gain

SUMMARY

Analysis of weight data of 3,230 patients indicates an average maternal weight gain of 23.2 pounds and a fetal weight gain of 7.4 pounds. The baby's birth weight is not related to maternal weight gain or loss unless the patient is diabetic or the gain excessive.

Post-partum weight loss is within 5 pounds of the total gain for all patients who gained the average poundage. But with excessive weight gain, 60 to 80 per cent of the weight gain in excess of normal will be retained, except in hydropic patients.

In general, it may be said that the amount of weight gained has relatively little effect upon the duration of labor, although excessive weight gain definitely increases the number of complications.

Weight gain per se is of little significance in the consideration of toxemia unless the weight gain is typed. The vast majority of all patients gaining an abnormal amount do not become toxemic. However, the toxemia incidence definitely rises as weight gain in excess of normal appears. Differentiation of hydropic from stereoplastic weight gain is of more value. For it is in the "edema group" (and most notably where edema is occult or nonstatic in type) that the incidence of toxemia is increased. Practically, however, sharp differentiation of the two is not always simple, and may depend upon clinical response to dehydration therapy in suspected weight gainers. Calculations of fluid retention, based upon fluid intake and urine output is of added value in deciding how to type such patients, to further the prognostic worth of weight observation.

39 GIFFORD AVENUE   .

Young, William C.: Observations and Experiments on Mating Behavior in Female Mammals, Quart. Rev. Biol. **16:** 311, 1941.

Extensive data on the behavior displayed at the time of estrus are now available for the rat, guinea pig, rabbit, sheep, cattle, pig, horse, cat, dog, howler, rhesus monkey and chimpanzee.

The generalization is warranted that each species displays a characteristic pattern of behavior with considerable individual variations. The latter are greatest among infrahuman primates.

In the mammals studied, estrous behavior has an endocrine basis. It is abolished by removal of the ovaries and restored by suitable replacement therapy. Ovarian action seems mediated by a neural center, or centers, in the hypothalamus or even farther back in the mesencephalon. Undoubtedly also additional physiologic factors are involved, social and environmental, in members of higher orders. Individual differences, that are a matter of age, or differences that may be of genetic origin, determine greatly the nature of the response.

HUGO EHRENFEST.

ADDITIONAL OBSERVATIONS ON MATERNAL PULMONARY EMBOLISM BY AMNIOTIC FLUID

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FATAL maternal pulmonary embolism by amniotic fluid and its particulate contents was described recently by the authors as a cause of obstetric shock and of other sudden deaths in, or following, parturition.[1] Clinically, the disease was characterized by profound shock which led in some cases to pulmonary edema, and in others was accompanied by uterine atony and hemorrhage. The essential pathology was found on microscopic examination of the lungs. It consisted of widespread embolism of small pulmonary arteries, arterioles, and capillaries by the particulate matter found in amniotic fluid and meconium. The disease was duplicated clinically and pathologically in dogs and rabbits by the intravenous injection of those substances obtained from human beings.

While that communication was in press, two additional obstetric deaths were found to be complicated by this form of embolism. Since they contain several features not seen in the 8 cases previously reported, they are presented here. These additions are (a) the subsequent fate of the emboli in women, (b) the sublethal form of this condition, (c) lanugo hair as embolus, and (d) such embolism in the absence of labor contractions.

CASE 1.—E. McI., white, 35 years old, para i, gravida ii, was a patient of Dr. Eloise Parsons at the Illinois Central Hospital, Chicago. She died seven days after delivery of a stillborn, full-term infant. Labor lasted about four hours, the second stage being twenty-five minutes and the third stage ten minutes. Subjective and visible labor pains were never strong, but she developed terrific pain in her right shoulder, became listless and the abdomen became sensitive early in the first stage. After delivery, which was accompanied by no excess hemorrhage, and was aided by low forceps, the patient was pale and continued to complain of pain in her shoulders and was nauseated and vomited several times. She received several blood transfusions, but her abdomen enlarged and a tender growing mass appeared in the right lower quadrant. She developed twitchings of the hands and generalized convulsions and died. The final clinical diagnosis was possible abdominal malignancy.

Post-mortem Findings.—Necropsy disclosed about 4,000 c.c. of bloody fluid and dark bloody clots in the peritoneal cavity. This seemed to have had its origin from a 3 cm. sized laceration through the left posterior uterine isthmus, the laceration involving the left uterine plexus.

There were no other important gross pathologic changes. The lungs together weighed 659 Gm. and grossly showed only a slight congestion. The heart weighed 250 Gm. The right ventricle was not dilated; the left was in systole. The abdominal organs were pale but not exsanguinated.

Histopathology.—Lungs: The principal pathologic findings were in small arteries, arterioles, and capillaries, many of which were occluded by masses of bluish-staining stringy material resembling mucin, or by an amorphous pink-staining substance, and occasionally by crescentic squamalike bodies. These materials were heavily infiltrated by large
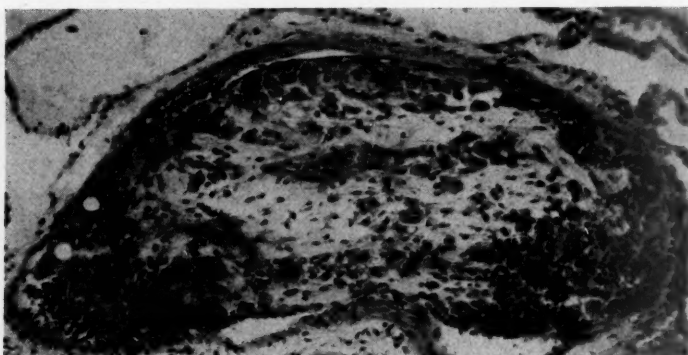
Fig. 1.—Pulmonary embolus of mucus and amorphous debris seven days after inception. Note macrophage and leucocyte reaction (Case 1). ×165.
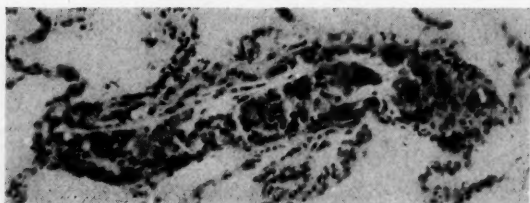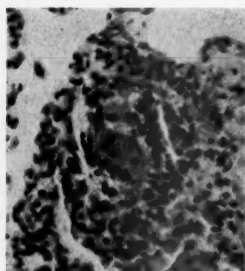
Fig. 2.   Fig. 3.

Fig. 2.—Mononuclear and multinuclear giant cells reacting to an embolus in an arteriole seven days after embolization (Case 1). ×165.

Fig. 3.—Panarteritis resulting from reaction to an embolus in small arteriole seven days after parturition (Case 1). ×165.

mononuclear macrophages, neutrophilic and eosinophilic polymorphonuclear leucocytes, and lymphocyte-like cells (Fig. 1). In some vessels there were in addition many mononuclear and multinuclear giant cells (Fig. 2). The cellular infiltration into some of the smaller emboli almost obscured them (Fig. 3). A refractile cylindrical body was seen occluding one vessel. Two giant cells were at one end of the structure. It contained some pigment granules and was similar in every respect to lanugo hair (Fig. 4). The inflammatory reaction sometimes involved the vessel wall and the adjacent lung tissue. The amount of embolism was moderate in comparison with that in the cases previously reported.

In addition, the lungs showed considerable emphysema and numerous megakaryocyte-like type of giant cell. There was no pneumonia or edema, but some acute hyperemia.

Uterine veins: A section through the region of the laceration in the left posterior segment of the uterine isthmus and the adjacent uterine plexus showed thrombosis of the blood vessels and hemorrhage into the areolar tissue. Some of the thrombi contained epithelial squamas, and showed beginning organization, as did the interstitial blood. Also located in the areolar tissue, as well as on the peritoneal surface and
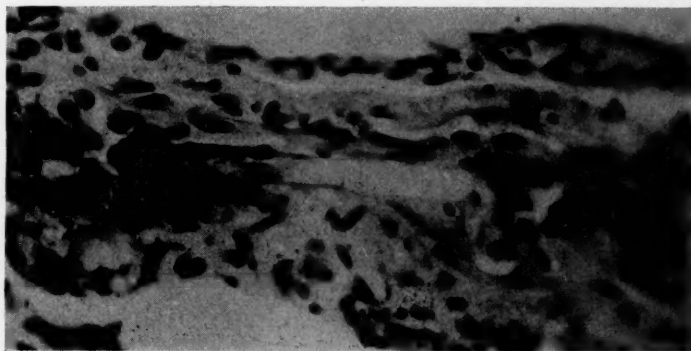
Fig. 4.—A lanugo hair seen as an embolus in an arteriole. Note giant cell reaction (Case 1). ×525.
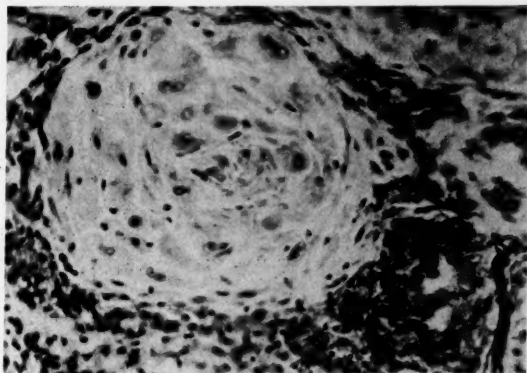
Fig. 5.—Small artery of omentum with cuff of decidual cells. Note sheet of squamas in lower right corner (Case 1). ×220.

directly in the laceration, were many similar squamas together with much mucuslike material. To these foreign substances there was an intense acute inflammatory reaction.

Omentum: A section through the omentum showed foreign bodies similar to those seen in the pulmonary and uterine vessels described above. There was an intense acute inflammatory reaction to them and to the free blood. In addition the capillaries and arteries were surrounded by a thick cuff of decidual cells (Fig. 5).

Miscellaneous: Liver and kidney sections were not remarkable. Sections of the brain showed small disseminated, sharply circumscribed foci of gliosis and one area of demyelinization.

Final Pathologic Diagnosis.—Massive intraperitoneal hemorrhage from rupture of the uterus. Pulmonary embolism by amniotic fluid. Multiple sclerosis.

CASE 2.—M. D., white, 38 years old, para ii, gravida iv, was a patient at the Chicago Lying-in Hospital. Because of a persistent hypertension which was not alleviated by treatment, she was admitted to the hospital
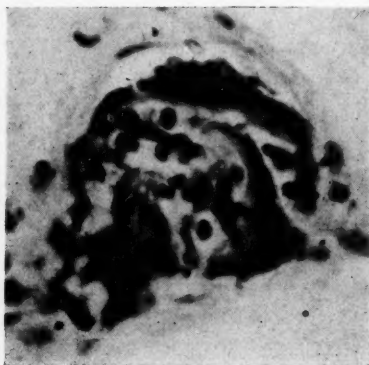
Fig. 6.—Squamas occluding an arteriole (Case 2). ×450.
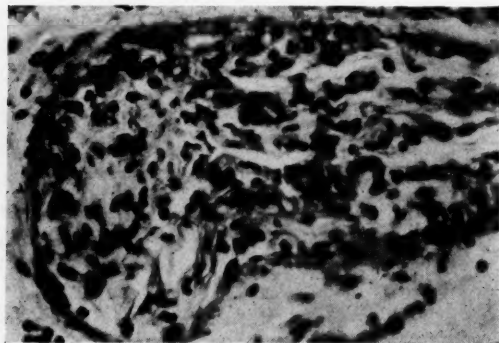
Fig. 7.—Mucus and squamas with leucocytic reaction occluding a small artery (Case 2). ×450.

near term. Her blood pressure ranged from 120-170/70-120. Her urine had slight traces of albumin. The quantitative albumin was 0.09 Gm./24 hr. specimen. Attempts at a medical induction were unsuccessful. Two days later painless bleeding occurred and examination revealed an anterior-lying total placenta previa for which a laparotrachelotomy was performed under local anesthesia. It was necessary to put the operating hand through the placenta and do a version and extraction with forceps on the aftercoming head of a living baby.

Following the operation the blood pressure and pulse were not obtainable. The patient was very pallid. Her breathing became gasping. She was given 500 c.c. of 20 per cent glucose, 500 c.c. of physiologic

saline, two blood transfusions, totaling 1,100 c.c., oxygen, and stimulants. The patient remained in shock. Pressure on the uterus, which had been packed, evacuated about 200 c.c. of blood and clots. She died about three and one-half hours after the operation began. The estimated blood loss was 800 c.c.

The final clinical impression was total placenta previa, toxemia, and laparotrachelotomy with hemorrhage.

Post-mortem Examination.—There was pallor of the skin and all abdominal organs. Both lower lobes of the lungs were atelectatic. The uterus was contracted. The operative incision was closed adequately. There was moderate pulmonary edema and hyperemia (lungs together weighed 600 Gm.). The left ventricle of the heart was contracted, but the right ventricle was remarkably flabby.

Histopathology.—Lungs: A few small arteries, arterioles, and capillaries showed occlusion by emboli which consisted of epithelial squamas and mucus (Figs. 6 and 7). There was an admixture of leucocytes in some of the mucus, and other vessels also showed a great excess of leucocytes. The total amount of embolism was small compared with the nine preceding cases.

The lungs in addition showed much emphysema, some edema, and focal atelectasis.

Miscellaneous: Kidneys: Sections showed some parenchymatous change. The glomerular tufts showed thickening of the endothelium. They were large and filled Bowman's space. Liver: Sections showed no abnormalities.

Final Pathologic Diagnosis.—Postoperative state following laparotrachelotomy for placenta previa. Toxemia of pregnancy (?). Minimal pulmonary embolism by amniotic fluid. Questionable exsanguination.

DISCUSSION

In neither of these two cases was there the picture of profound, sudden shock which was described in the previous paper. This is in accordance with the amount of embolism which was seen on microscopic examination of the lungs. In both of these two women, this was less than in the previous eight cases. In Case 1, the effects of the embolism appear to have been subclinical or masked by the symptoms due to the ruptured uterus. In Case 2 death appears to have been due to vasomotor collapse in which the relative importance of hemorrhage, operative trauma, pulmonary embolism, and possibly nonconvulsive toxemia cannot be determined in retrospect. This case, then, may illustrate the point previously made that the effects of this form of embolism may be obscured by a combination of causes, and that these might lead to death, whereas each alone might be survived.

Case 2 illustrates that embolism of the lungs by the particulate materials in amniotic fluid can occur in the absence of labor pains if a route is provided by other means, in this case, incision through the placental site. However, since the amount of embolism seen in this case was distinctly less than that in the other nine cases, it tends to fortify our opinion that strong or excessive labor pains are an important predisposing factor.

In our previous paper we made considerable efforts to determine the origin of the emboli materials found in the lungs. We concluded that the emboli represented the epithelial squamas and vernix caseosa found in the amniotic fluid together with the meconium present there in some cases. The presence of lanugo hair, as an embolus (Fig. 4), further supports this view.

The large amount of decidual reaction present in the omentum in Case 1 in the presence of intraperitoneal amniotic fluid raises the question of its etiology. Such reactions have been described by Williams,[2] Harbitz,[3] and others. It is the subject of further investigation.

The reaction to the pulmonary embolic materials at seven days was less severe than we had anticipated following our observations on dogs. In these experiments, however, the amniotic fluid and meconium used to embolize the lungs had not been kept sterile, and bacterial infection might, therefore, be responsible for part of the intense reaction illustrated at seven days in our previous paper. The type and amount of macrophage reaction indicates that these materials act approximately like many other aseptic foreign bodies, and that their subsequent fate would probably be complete removal. The mucus was already difficult to identify as such as seven days. The reaction to it was mainly that of macrophages. The squamas and amorphous materials caused a marked foreign body giant cell reaction.

SUMMARY

Two additional cases of maternal pulmonary embolism by amniotic fluid are presented. Lanugo hair is illustrated as a component of the embolic material. Existence of the sublethal form of this condition is shown and the subsequent fate of the human emboli is found to be approximately similar to that described by us in experimental animals. The occurrence of this phenomenon following laparotrachelotomy in the absence of labor contractions is reported.

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By means of a photograph of the five babies and of the official birth certificate made out by the attending physician, another instance of quintuplets is placed on record. The five children were all boys, one of them stillborn, the other four dying soon after birth. Their aggregate weight was ten pounds two ounces, and the birth certificate stated that there was but one placenta.

HUGO EHRENFEST.

THE EFFECT OF NICOTINE ON LACTATION IN WHITE MICE

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STUDY of the hormone levels during pregnancy and the puerperium suggests an endocrine control of lactation. While this supposition may be true, there are other factors, the blood and nerve supplies to the gland, which play an important part in determining the ability of the breast to function adequately.

In the quiescent state, the blood flow through the gland is sufficient to maintain normal tissue metabolism. Prior to the onset of lactation there is a marked vascular engorgement of the breasts; this increased blood flow continues, but is somewhat less pronounced, during the period of secretory activity. Since the synthesis of milk is dependent upon the materials provided by the blood stream, an increased blood flow through the gland is necessary for the maintenance of lactation and conversely a diminution in the blood flow might compromise the secretory activity of that structure. Although the action of nicotine on the blood vessels of the breast has not been subjected to specific study, it is assumed that the vascular effects are the same as noted in other parts of the body, that is, a peripheral vasoconstriction with a diminution of blood flow and a drop in surface temperature.[1-3]

In the human being, the nerves supplying the breast come from the fourth, fifth, and sixth intercostals; the accompanying sympathetic fibers pass by way of the grey rami communicantes from the thoracic portion of the sympathetic system to plexuses upon the basement membrane about the alveoli. Nerve endings have been demonstrated between the secretory cells in the gland. Although nerve control of lactation has not been confirmed, it is possible that some influence may be exerted through these pathways, since secretion in other glands is a direct result of nervous impulses. Nicotine acts on the ganglia of the secretory nerves, its action consisting of an initial stimulation followed by complete paralysis and cessation of secretion.[7] This effect has been demonstrated on the salivary, sweat, mucus, and adrenal glands both by local and general administration of the drug.

Any inadequacy of milk production in human beings may be compensated for by the substitution of an artificial formula. In animals, however, the inability of the mother to secrete enough milk to provide for the demands of the litter will evidence itself either in death of the weaker young or in undernutrition of the whole group.

A few attempts have been made to determine the effects of the administration of nicotine on lactation and animal growth.

Behrend and Thienes[4] and Thienes[5] have shown that large doses of nicotine given to young animals which are adequately nourished have no effect on subsequent growth and development. Essenberg, Schwind and Patras[6] gave nicotine to pregnant rats by several methods and found that two-thirds of the young were underweight and that many entire litters were lost by death, abortion, or resorption of the fetuses. Their use, however, of doses large enough to produce convulsions in the animals studied naturally confuses the results, since the fetuses may have been actually poisoned by the drug.

This study was undertaken in an effort to demonstrate the effects of the administration of nicotine on milk production as evidenced by the weight gains in a standard-sized litter of offspring, during a two and one-half weeks' period of lactation. Thirty-six pairs of immature white mice from our laboratory stock were selected for the study and were followed through three consecutive litters.

The average daily water intake of the animals was measured over a period of one week before the experiments were started. The nicotine was then supplied to the animals in the drinking water in a solution of a strength to furnish 0.5, 1.0, or 2.0 mg. in the daily fluid intake. Although the amounts of the drug ingested undoubtedly varied from day to day, the average intake over the period the animals were followed approximated the anticipated amount, since checks on the daily fluid intake revealed it to be at an almost constant level. Other methods of administration of the drug, by injection or the use of cigarette smoke, were considered. Both were eliminated in favor of the one utilized, because nicotine is absorbed readily from the gastrointestinal tract and frequent ingestion of small quantities would maintain a more constant supply in the tissues. Other factors concerned in the choice were the ease of administration and the fact that a much larger daily dose could be utilized.

Of the 36 pairs of mice studied, 12 pairs were used as controls and were given tap water; 10 pairs, 0.5 mg.; 8 pairs, 1.0 mg.; and 6 pairs, 2.0 mg. of nicotine daily. The litters were reduced arbitrarily to six on the day of birth and each group was weighed at birth, at one week, at two weeks, and at two and one-half weeks of age, and the average individual weight obtained. An accurate account of the initial litter size and the ultimate mortality of the offspring was recorded.

RESULTS

Litter Size.—The average number of offspring in each litter was reduced slightly in the groups to which the drug was administered. The largest litters were born to the control animals and to those receiving 0.5 mg. of the drug, and the smallest to those receiving 2.0 mg. daily.

Since the litter size consistently decreased in the animals to which the larger doses of the drug were given, the change probably may be interpreted as the result of the effects of the nicotine. Although the reduction was definite and occurred in each litter in the groups receiving nicotine, a larger series might alter the figures. (Table I).

TABLE I. INITIAL LITTER SIZE

GROUP	AVERAGE NUMBER OF OFFSPRING PER LITTER		
	LITTER 1	LITTER 2	LITTER 3
Control	9.0	11.2	10.4
0.5 mg.	9.4	10.9	10.5
1.0 mg.	8.8	9.0	9.0
2.0 mg.	7.0	8.0	8.0

Mortality.—The mortality rate was high for all groups. This may have been due to the trauma occurring with the removal of the young from the nests on the day of birth for weighing and reduction of the litter size. Although great care was taken, injury may have occurred in some instances. The figures (Table II) reveal a marked variation in

TABLE II. MORTALITY OF OFFSPRING

GROUP	MORTALITY RATE PER LITTER		
	LITTER 1	LITTER 2	LITTER 3
Control	34.5%	27.8%	31.0%
0.5 mg.	33.7%	46.2%	31.6%
1.0 mg.	33.0%	8.3%	46.4%
2.0 mg.	22.5%	16.6%	6.7%

the death of the young with no apparent regard to the amount of the drug ingested. Although the mortality is high, the variation is not inconsistent with the death rates seen in normal groups of untreated mice. The facts that the lowest average mortality in this series occurred in one group of the animals receiving the most drug and that the control group showed a consistently high death rate suggest that factors other than the nicotine played a large part in the loss of the young.

Weight.—The weights of the offspring at birth (Table III) were almost identical for each of the four groups studied, indicating that the administration of the drug in doses below a severely toxic level has no effect on the intrauterine development of the fetuses.

TABLE III. BIRTH WEIGHT

GROUP	AVERAGE BIRTH WEIGHT (GRAMS)		
	LITTER 1	LITTER 2	LITTER 3
Control	1.4	1.35	1.5
0.5 mg.	1.3	1.4	1.25
1.0 mg.	1.4	1.5	1.5
2.0 mg.	1.5	1.4	1.4

The weight curves for each litter of the four groups demonstrate a fairly normal and constant gain. In the first litter (Fig. 1), the offspring from the animals taking 1.0 and 2.0 mg. of nicotine daily weighed
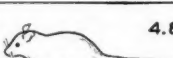
	I WEEK	2 WEEKS	2½ WEEKS
CONTROL	4.5	6.2	7.9
0.5 MG	4.7	7.3	8.2
1.0 MG	2.7	4.0	4.6
2.0 MG	3.3	4.8	5.1

Fig. 1.—Litter 1. Average individual weight (Gm.).

	I WEEK	2 WEEKS	2½ WEEKS
CONTROL	3.5	5.7	6.5
0.5 MG.	4.0	6.2	6.6
1.0 MG.	3.9	5.1	5.8
2.0 MG.	4.8	6.0	7.0

Fig. 2.—Litter 2. Average individual weight (Gm.).
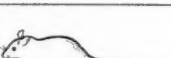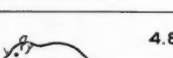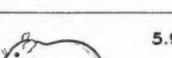
	I WEEK	2 WEEKS	2½ WEEKS
CONTROL	3.5	5.4	5.5
0.5 MG.	3.5	5.7	6.1
1.0 MG.	3.1	5.2	4.7
2.0 MG.	4.8	5.9	7.1

Fig. 3.—Litter 3. Average individual weight (Gm.).

less than those getting 0.5 mg. of the drug or only water. That this difference was not an effect of the drug is shown by the weights in the second litter (Fig. 2); the offspring of all the groups except those to which 1.0 mg. was given weighed about the same. In the third litter (Fig. 3), the young from the parents receiving nicotine in daily doses of 0.5 and 2.0 mg. outgained the rest. Again as in the previous two litters, those getting 1.0 mg. produced the lightest offspring.

DISCUSSION

Since it has been demonstrated that the administration of nicotine to young normal animals has no effect on their rate of growth and development[4-5] any changes produced when the drug is given to the parents must be on the basis of alteration of the milk supply rather than by the nicotine excreted in the milk. The fact, shown in this study, that the weights at birth of offspring of mice being given relatively large doses of nicotine are the same as those of the controls indicates that the nicotine has little or no effect on the intrauterine development of the animals.

The difference in weight curves in the first litter is not very significant since this difference is observed commonly in groups of normal animals at the onset of their reproductive careers. In the second and third litters, two groups of the treated animals showed gains greater than those of the control group, suggesting that in this particular test animal nicotine has little effect on the amount or quality of the milk produced. The group to which 1.0 mg. of the drug was given consistently produced lighter offspring than the other groups. Since the ability to lactate varies considerably with individuals, this observation must be interpreted as a physiologic variation rather than inhibition of lactation by nicotine.

At no time was any alteration in behavior noted. The young were cared for normally in all instances and there was no obvious increase in cannibalism in the nicotine-treated animals as occurred in the groups studied by Essenberg, Schwind, and Patras.[6]

CONCLUSIONS

1. The effect of nicotine on lactation as evidenced by the weight gains in the offspring was studied in white mice. The animals were treated with 0.5, 1.0, or 2.0 mg. of the drug daily through three consecutive litters.

2. A slight but consistent reduction in litter size was noted with increasing doses of the drug.

3. No remarkable differences in mortality rate, birth weight, or weight gain during the period of lactation could be demonstrated between the controls and the treated animals.

4. A marked variation in all the above factors was noted within each individual group.

5. The ingestion of nicotine results in no impairment of lactation in white mice.

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PARALDEHYDE IN OBSTETRICS, WITH PARTICULAR REFERENCE TO ITS USE IN ECLAMPSIA*

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IN 1934 we began to use paraldehyde at the University Hospital as an analgesic in labor and found it to be quite satisfactory. After a period of trial with the rectal route, which had its obvious disadvantages, we started oral administration and here the results were even better. In 1938 we published a report of 350 cases and in it stated that, in our opinion, paraldehyde was the safest and most satisfactory analgesic available at that time.

Since the publication of this report we have continued to use this drug. In the large majority of the cases it is given by mouth and mixed with aromatic elixir to partially disguise the taste. Other clinics are using fruit juices, water or some other medium and one seems to be about as satisfactory as another. It would appear to be important that the mixture should be thoroughly chilled and swallowed quickly, in order to lessen the disagreeable taste and prevent vomiting. Should the latter occur, a second dose given some fifteen minutes later is usually retained and the desired effect results.

It has continued to be our custom to precede paraldehyde by a small dose of one of the barbiturates (e.g., pentobarbital sodium, gr. 3), and we feel that the action of the drug is enhanced somewhat thereby. On the other hand, this is not an inflexible rule, and is not followed in all clinics, some physicians feeling that there is an increase in fatal asphyxia when the combination is used. While our experience does not bear this out, we believe that the point is quite minor and not worthy of any discussion.

The time of administration of paraldehyde varies in different clinics, it being our custom to give it when the patient feels that she wants relief. Should she be of the type who demands or expects analgesia from the onset of pain, her request is not answered until labor is well established, for it is in these cases that we find that the duration of labor is sometimes prolonged.

While not constant, the usual initial dose of paraldehyde is 5 or 6 drams in an equal amount of aromatic elixir. Good effect should occur within fifteen minutes and maximum in one-half hour. Duration is about six hours, and the original or a smaller dose may be given at this time if needed. In those patients in whom the drug is given by rectum, the dose is larger, 8 drams of paraldehyde in 5 or 6 drams of mineral or olive oil being used. Here, the effect is slower, one hour being required for maximum effect, and the duration is about the same. Again, repeat doses are quite permissible.

The effect of paraldehyde varies somewhat. The majority of the patients fall into a deep sleep with continuation of their labor. They are usually moderately restless with pains and quiet in the intervals. A few are more restless, roll from side to side and would probably fall out of bed without some preventive, such as bed sides. In another group there appears to be little or no loss of consciousness nor relief from pain, and the drug would seem to have failed entirely, yet later it is found that the patient has no recollection at all of anything that happened after she received it. And finally, in about 5 per cent of the cases the method fails to produce either amnesia or analgesia. One of the major contributing factors to failure is a full stomach, labor having started shortly after the ingestion of a full meal and having progressed rapidly. The greater number of these patients have a very short labor, and the need for relief is not great.

The analgesia seldom reaches the point of surgical anesthesia, so that while spontaneous delivery is satisfactorily carried out and while the incidence of operative delivery is not increased, should the latter be decided upon, some additional method of pain relief is needed. Paraldehyde does not prohibit the use of any of the general anesthetics, indeed the amount needed for complete anesthesia is less than without it. Or, should it be desired to complete the delivery under local or regional anesthesia, this can also be done without added risk.

Effects other than those noted above are not many. The pulse rate is almost routinely increased, but not alarmingly so. Paraldehyde is an extremely safe drug, and we have not had a maternal death, or major accident which could in any way be attributed to it.

From the standpoint of the infant, it is probably safer than any other drug used. While paraldehyde can often be detected upon the baby's breath, most cry spontaneously and any depressing effect dis-

appears rapidly. Resuscitation, when required, is easy and recovery complete. The one exception to this would appear to be the quite premature infant, weak and sickly at best and ill equipped to withstand strain of any kind. In this group the incidence of severe asphyxia is somewhat, though not greatly, increased.

There is another use for paraldehyde in obstetrics that is mentioned at times, but has never been greatly emphasized. This is as a means of producing sedation in eclampsia and pre-eclampsia. To us, this is most important and has not received the attention it deserves. In pre-eclampsia, paraldehyde will quiet the patient more satisfactorily than any sedative used today, and will permit of time to establish whatever routine treatment is desired. Or, should she be in labor, this may continue to termination under its influence without fear of the onset of convulsions. It must be understood that, for this result, the patient must be kept very well sedated and the physician must not hesitate to repeat the drug as often as necessary. Large doses are tolerated very well, and are often required.

It is in the field of eclampsia itself, however, with frequent convulsions, that the value of paraldehyde stands out so prominently. In reading the literature on the treatment of eclampsia, it is found that practically every writer today advocates the conservative method; yet, it is almost invariably stated that should it be impossible to control convulsions by whatever method of sedation is recommended, this form of therapy should be abandoned and operative delivery undertaken. It is stated that this definitely increases the risk and raises maternal mortality, but that a continuation of an unsuccessful type of treatment would give worse results. All of this is quite evident and would need no comment except for the fact that it is our experience that *paraldehyde, in sufficient dosage and repeated often enough, will, without exception, prevent convulsions, keep the patient quiet, and lower the blood pressure.* This last effect, the lowering of the blood pressure, is not outstanding, but there is usually a drop of some 40 to 50 mg. hg, both systolic and diastolic. The pressure has a tendency to remain at the new level for several hours, and then to rise rather gradually. All of this is accomplished with a minimum of risk to both mother and baby.

In 1936 we began to use paraldehyde as the main sedative agent in the treatment of eclampsia, and as time has elapsed have depended more and more upon it for this effect. Our results on the whole have been so encouraging that it was felt that they should be reported although the total number of cases (48) is small.

It must be understood that we are not attempting here to give the treatment of eclampsia, but merely to emphasize the advantages of paraldehyde to produce sedation when this is desired.

The routine followed in all cases is to give paraldehyde rectally in an initial dose of 10 drams in 5 or 6 drams of olive or mineral oil as soon after admission as possible and then to start intravenous concentrated glucose and other therapy. The rectal route is forced upon us by the fact that these patients are unconscious and unable to swallow. The oral would be preferable because of the more rapid absorption and ease of administration. The patients are watched constantly, blood pressures being taken every one-fourth to one-half hour and if restlessness is returning as the effects of the paraldehyde wear off, the dose is repeated. This is continued until the acute stage has passed and the patient is quiet or conscious without the drug. No attempt is made to induce labor in the ante-partum group until danger of convulsions is past, but if the patient is in labor or if labor begins, it is allowed to continue as normally as possible, only absolutely indicated operative work being done and this invariably without inhalation anesthesia. In this series the majority of the patients either were in labor on admission or went into labor spontaneously; however, five recovered from the acute attack, became conscious and rational, but continued to show marked evidences of toxemia, as manifested by hypertension and urinary findings. These we classified as posteclampsia, in contrast to pre-eclampsia, and in this group the uterus was emptied in what seemed the most conservative manner. There seems to be no precedent for the term "posteclampsia," but the need of some designation is evident. The patient no longer has eclampsia; however, she continues to have a toxemia, and is far from complete recovery.

For purposes of comparison we have tabulated 49 consecutive cases of eclampsia which received no paraldehyde but were in other respects treated about the same. The two series are quite comparable in that in each there were 15 cases classified as severe eclampsia, in the paraldehyde group 20 were moderately severe and 13 mild, in the nonparaldehyde these figures were 26 and 8, respectively; and there was also little difference in the time of onset, in the first instance (paraldehyde) 24 were ante partum, 13 intra partum, 10 post partum, and 1 both intra and post partum. In the second series these figures were 21, 15, 12 and 1.

It is when we begin to compare results that the great differences are noted.

In the nonparaldehyde group, 32 of the 49 patients, almost two-thirds, continued to have convulsions in spite of vigorous sedation with the accepted drugs. The number of convulsions after beginning treatment were usually between 1 and 10, one patient having 23 and another 49. The greatest number of convulsions before treatment was started in this group was 9. Comparing these figures with those patients treated with paraldehyde, we find these interesting facts: When we first began to use the drug we were prone to give too small an initial dose and to

delay repeating it as early as it should be repeated. In this group of 22 patients there were 6 who had either one or two convulsions after sedation was begun, about one-fourth as compared to two-thirds in the nonparaldehyde group. The remaining 26 patients received an adequate amount of paraldehyde, and in this group the percentage of failure was zero, no convulsions occurring after sedation had been obtained. Included in this group we find that one patient had 12, one 16, while a third had 28 convulsions before receiving paraldehyde and none after. The amount of the drug necessary to control the convulsions varied from a minimum of 12 to 15 drams to a maximum of 120 drams in one case and 131 drams in another, both over a period of three to four days. As an interesting side light, the latter patient went into labor after some four to five days of treatment and delivered herself of a premature living child. Both mother and baby did well and were discharged from the hospital in good condition some two weeks post partum. At the time of writing this report, she is again a patient of ours, having passed through this second pregnancy with no evidence of toxemia and delivering at term without incident. Both babies are alive and well.

It is our feeling, therefore, that paraldehyde, in sufficient amounts, will absolutely control the convulsions of eclampsia and permit of a continuation of the conservative treatment for an indefinite period of time, whether this be hours or days.

The maternal mortality in the nonparaldehyde group was 7, or 14.29 per cent, and in the second group there was one death, or a 2.08 per cent mortality, this death occurring from bronchopneumonia several days after delivery and recovery from the eclampsia.

Fetal mortality in the nonparaldehyde group was 14, or 28.58 per cent, and in the other 11, or 22.95 per cent, in both instances the figures being uncorrected. These figures would seem to indicate that, by the use of paraldehyde, we have materially reduced the maternal mortality in eclampsia and have not accomplished this at the expense of the baby.

Smith, Earl Conway: Sodium Perborate Therapy in Trichimonas Vaginalis Vaginitis, New Orleans M. & S. J. 94: 37, 1941.

A safe, simple, economical, and prompt method seems to have solved the problem of therapy in *Trichomonas vaginalis* vaginitis, according to Smith. The patient is instructed to douche with a weak lactic acid solution which is followed by the insertion of 10 gr. of sodium perborate in a veterinary capsule daily for fifteen days. Thereafter for seventy-five days the patient continues daily douches of either lactic acid or sodium perborate, depending upon the pH of the vaginal secretions. The patient is discharged as cured when smears show the absence of the organism after three consecutive menstrual periods.

EUGENE S. AUER.

INTRAVENOUS ADMINISTRATION OF BASERGEN DURING THE THIRD STAGE OF LABOR

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A NUMBER of recent reports contend that the ergot alkaloid ergonovine, when administered intravenously immediately after the birth of the baby, not only shortens the third stage of labor but materially reduces the loss of blood. We have studied the action of this drug in this respect in a series of 400 patients and wish to report briefly our findings.

PROCEDURE

The preparation used by us was Basergen,* a water-soluble tartrate of ergonovine, $C_{19}H_{23}O_2N_3$.

As quickly as possible after delivery of the baby 1 c.c. (0.2 mg.) of the drug was given intravenously, usually by the anesthetist. Although the lapse of time between the completion of the second stage and the administration of the basergen varies, the interval rarely exceeded one to two minutes. Within one minute after the injection, expression of the placenta was attempted. An occasional delay of one or two minutes occurred whenever there was no assistant available to tie the cord. While it was necessary in most instances to express the placenta by compressing the anterior and posterior surfaces of the uterus, spontaneous expulsion within two minutes after the administration of basergen was by no means uncommon.

In a control series of 200 patients no attempt was made to expedite the separation of the placenta. In this group, the placenta, after spontaneous separation, was expressed by pressure on the fundus, and the patient was then given an injection of 1 c.c. each of ergone and posterior pituitary extract. The time of placental expulsion as well as the loss of blood were recorded for comparison.

Both groups comprised a consecutive number of patients regardless of the method of delivery, cesarean sections being excluded.

DURATION OF THE THIRD STAGE

As recorded in Fig. 1, a definite shortening of the third stage of labor occurs in an appreciable number of patients when basergen is given. A third stage longer than ten minutes occurred in only 12 per cent of the basergen group, as compared to 36 per cent of the controls. In other words, 88 per cent of the basergen patients against 64 per cent of the controls experienced a third stage of ten minutes or less. A third stage of five minutes or less occurred in 59 per cent of the basergen patients as against 25 per cent of the controls.

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*A product of the Sandoz Chemical Works, Inc., New York.

BLOOD LOSS

The blood loss during the third stage was estimated, not measured. However, since this procedure was used in both series the inaccuracy is less objectionable and permits comparison. According to our observations, there was no apparent difference in the loss of blood in the two groups, which is contrary to several recently published reports. We encountered no systemic reactions from basergen.

Tritsch and Behm[1] report in their series that "80 per cent had definitely less than average bleeding after the delivery of the infant and placenta," although 3 cases (2.6 per cent) of profuse bleeding were recorded. Adair and his associates,[2] in a series of 51 patients, found an average blood loss of 100 c.c., the maximum loss being 300 c.c. in 86 per cent of cases, while 13.7 per cent experienced a loss of 500 c.c. or over, but there were no control cases in their series.

		Basergin (400):	Controls (200):
1.	Duration 10 min. or less:	88.00%	64.0%
2.	Duration 10 to 30 min.:	11.50%	34.5%
3.	Duration 1 hour or more:	0.50%	1.5%
4.	Longest third stage:	1 hr., 13 min.	2 hours
5.	Retained placentae:	2.50% (10)	0.5% (1)
6.	Manual extractions:	2.50% (10)	0.5% (1)
7.	Operative deliveries:	19.75% (79)	13.0% (52)
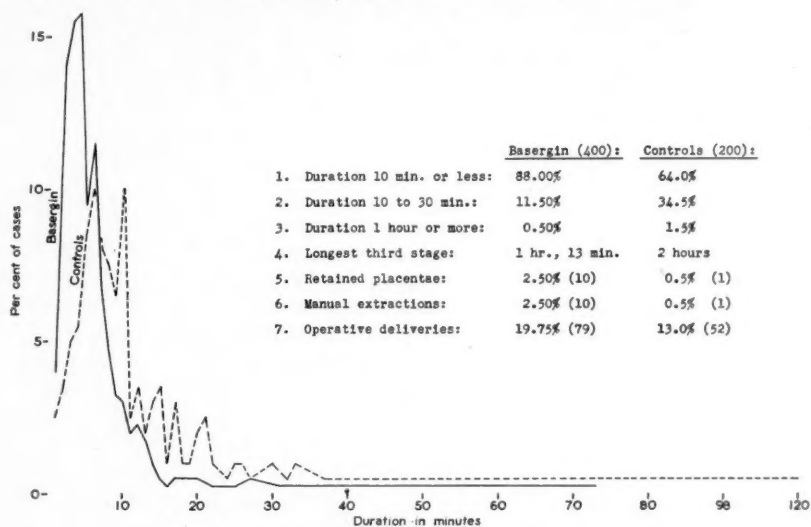
Fig. 1.—Duration of third stage.

Reich[3] reports a series of 154 cases in which ergonovine was administered intravenously during the second stage of labor. Of these, 55.8 per cent lost less than 100 c.c. of blood, as against 28.8 per cent of the controls. No hemorrhages over 900 c.c. occurred in those receiving ergonovine, as compared with 9 cases in the control group. In another group of 588 cases in which ergonovine was given after the third stage, Reich noted a loss of 500 c.c. or over in 7.1 per cent as against 16.1 per cent in 548 control cases, where ergotamine tartrate was given.

In our series, a loss of 300 c.c. or less of blood was noted in 92 per cent of the basergen group as compared with 93.5 per cent of the controls; 300 to 500 c.c. were noted in 7 per cent of the patients given basergen and in 6 per cent of the control series. And finally, a severe hemorrhage of over 500 c.c. occurred in 1 per cent of the basergen patients and in 0.5 per cent of the controls (Fig. 2).

RETAINED PLACENTAS

Retention or incarceration of the placenta, due to uterine tetany, may occur after the use of any ergot derivative. This is the one serious

objection raised to the routine use of these drugs. In our experience manual removal of the placenta was necessary in 10 out of 400 patients, an incidence of 2.5 per cent. In the control group this occurred only once in a series of 200 patients (0.5 per cent). Nine of the placental retentions were due to tetanic contraction of the lower uterine structures. Only in one instance was it due to uteroplacental fusion. However, no difficulties were encountered in the extraction of the placentas from the lower uterine segment. If, when basergen is given, the operator places his or her hand over the fundus and exerts moderate pressure on the fundus as soon as contractions are noticed retention of the placenta is less likely to occur.

	Basergin	Controls
1. Blood loss 300 cc. or less:	92%	93.5%
2. Blood loss 300 - 500 cc. :	7%	6.0%
3. Blood loss over 500 cc. :	1%	0.5%
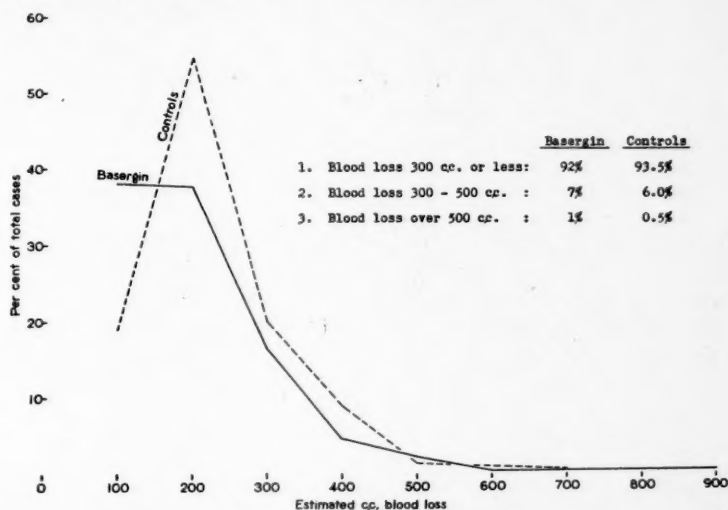
Fig. 2.—Blood loss in third stage.

All but three of the cases requiring manual removal of the placenta presented some abnormality, as indicated in Table I. It is noteworthy that the blood loss in 8 of the 10 cases was less than 300 c.c., in one it amounted to 350 c.c., and one may be considered as an instance of post-partum hemorrhage, since it was 500 c.c. None of the patients in this group developed post-partum fever.

TABLE I

CASES OF MANUAL REMOVAL OF PLACENTA	PLACENTA RETAINED MIN.	BLOOD LOSS C.C.
Basergen Series:		
Case 1: Twins	25	200
Case 2: Premature	5	100
Case 3: Breech	15	100
Case 4: Premature, L.A.D.A.	28	500
Case 5: R.O.P., Manual rotation	36	100
Case 6: Uneventful	4	200
Case 7: Uneventful	73	100
Case 8: Uneventful	42	200
Case 9: R.O.A., low forceps	3.5	350
Case 10: Adherent placenta	31	100
Control Series:		
Case 1: Persistent occiput posterior	98	350

Reich, using ergonovine intravenously during the second stage of labor found, in a series of 154 cases, retained placenta in four instances (3.85 per cent) which necessitated manual removal. Tritsch and Behm similarly report an incidence of 3.47 per cent of retained placenta in a series of 115 cases.

CONCLUSIONS

1. The intravenous use of basergen at the end of the second stage of labor shortens the duration of the third stage.

2. With the exception of about 1.5 per cent of the patients treated, this procedure does not bring about any appreciable decrease in the volume of blood loss in the third stage.

3. Contraction of the lower uterine segment necessitating manual extraction of the placenta is definitely increased after intravenous basergen administered at the end of the second stage.

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2398 SACRAMENTO STREET

THE TREATMENT OF STERILITY WITH "SMALL DOSE" X-RAY THERAPY

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THE treatment of functional menstrual disorders and sterility by irradiation of the ovaries and pituitary gland with small doses of roentgen rays (so-called x-ray stimulation) has been described by many. In 1939, Kaplan,[1] and Mazer and Baer[2] analyzed fifty-two articles on the subject and described their own extensive experiences. From these reports, they concluded that small-dose irradiation appears to be of distinct therapeutic value in the treatment of irregular menses, amenorrhea, and sterility.

In the face of this evidence, it is surprising to find that this type of therapy is not attempted with greater frequency. Some of the reasons for this are: the belief that x-rays are not effectual in restoring an endocrine imbalance; that many of the reported successes are chiefly coincidental; and the fear of damage to the offspring.[3-9]

The following case of sterility is therefore presented again[10] and brought up to date because of the comprehensive clinical and laboratory

evidence of the nature of the endocrine imbalance, and because of the apparently repeated successful responses following small dose x-ray therapy.

<center>REPORT OF A CASE</center>

Mrs. E. P., white, aged 26 years, first sought medical attention on May 21, 1935, because of menstrual irregularities of thirteen years' duration and sterility of six years' duration. Her menses began at the age of thirteen, were generally scant, and averaged six to eight periods a year. Since her marriage, six years prior, there were four episodes of amenorrhea lasting six to seven months each. Occasionally there had been a hemorrhage lasting about one week, and, for the past eight weeks, there had been continuous staining (see Fig. 1). Previous treatment for her sterility had been unsuccessful.

Physical examination revealed an obese patient weighing 215 pounds with a fat distribution suggestive of pituitary deficiency (girdle obesity, apronlike abdomen, narrow ankles and wrists, scant pubic and axillary hair). Examination of the pelvic organs revealed a slightly enlarged right ovary. Rubin and Hühner tests were normal. The husband's spermatic fluid was found to be normal. Roentgenographic examination of the skull revealed a normal sella turcica.

The patient was given the following hormone therapy in 1935 without benefit: oral medication with anterior pituitary extract (5 gr. emplets); thyroid extract (0.25 gr.) 3 times daily for one month; intramuscular injections of A.P.L. (anterior pituitary-like hormone) (2 c.c. each) twice weekly for one month; three courses of injections of prephysin given in December, 1935, January, and February, 1936, each course consisting of 1 c.c. daily for ten days; the last course was followed by 3 injections of progynon-B (2,000 R. U. each) in one week; and in March, 1936, the patient received 3 bi-weekly injections of A.P.L. (2 c.c. each). In spite of this treatment, the menses remained irregular (see Fig. 1).

A comprehensive endocrine study was conducted. Four endometrial biopsies were taken on March 30, April 6, May 29, and June 4, 1936. The first one, taken on March 30, showed only moderate luteinization, but, the one taken the following week, instead of showing more advanced luteinization, showed a proliferative phase. The third biopsy was deferred for three weeks in order to study the same phase in a succeeding menstrual period. It was taken on May 29, and showed very slight luteinization. Once again the following biopsy showed only a proliferative endometrium. Thus the endocrine imbalance consisted in part of an incomplete or abortive luteinization process. At four consecutive intervals of about one week (May 12, 19, 28, and June 4, 1936), bio-assays of twenty-four-hour specimens of urine, taken during the middle of a two-month period of amenorrhea, failed to reveal any prolan or estrin, except for 13 rat units of estrin in the last specimen (see Fig. 1). Two of the aforementioned endometrial biopsies were taken on the same day as the last two bio-assays. It was decided to administer small dose x-ray therapy.

Four x-ray treatments were given from June 25 to July 5, 1936, delivering in four treatments a total dose of 80 roentgens (measured with back scattering) to the pituitary gland and 80 roentgens to each ovary. One month later, the patient began to menstruate regularly once a

month for the first time in her life. After the third regular menstrual period, it was decided to determine whether the restored monthly bleeding was accompanied by normal cyclical endometrial changes. Consequently, on the day preceding the fourth expected period (Oct. 29, 1935), a premenstrual endometrial biopsy was taken.

In the microscopic examination of this endometrium, Dr. William Antopol found "endometrium in lutein phase with an early embryo." A detailed study of this embryo by Scipiades[11] at the department of
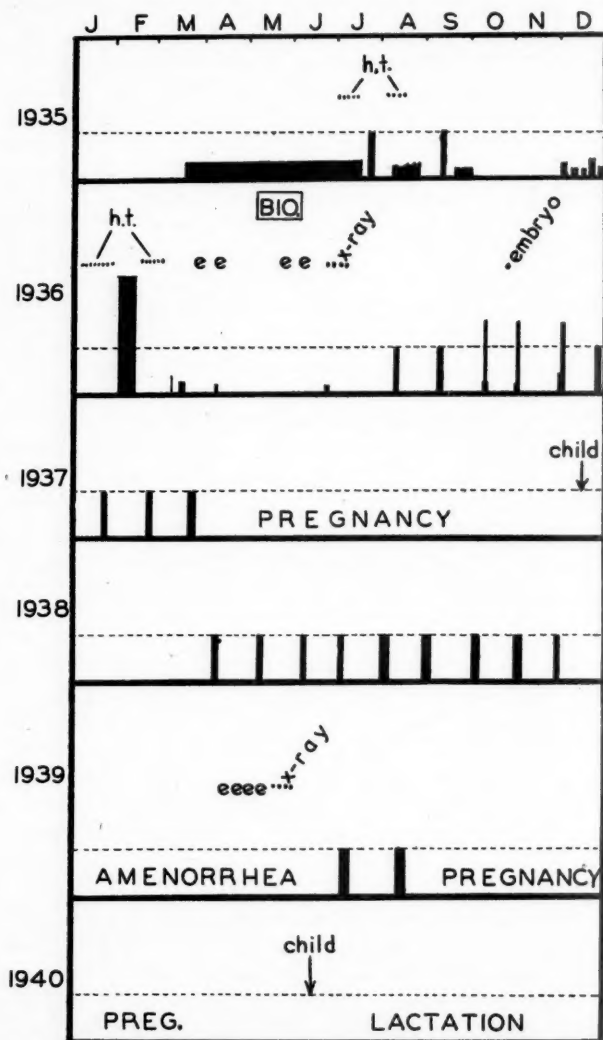
Fig. 1.—Monthly menstrual chart, illustrating clinical course over a period of six years. The solid blocks represent menstrual flow; the broken line represents the normal level of menstrual flow. 1935: Menometrorrhagia alternating with amenorrhea; *H.T.*, hormone therapy. 1936: *H.T.*, hormone therapy, associated with a severe hemorrhage; *E*, endometrial biopsies which showed incomplete luteinization; *Bio.*, bio-assays of prolan and estrin in the urine (see text); *X-ray*, small dose x-ray therapy; *Embryo*, accidentally removed by suction curettage (see text). 1937: Normal child born in December. 1938: Regular normal menses. 1939: Amenorrhea characterized by absence of lutein effect as shown by four weekly endometrial biopsies (E); *X-ray*, small dose x-ray therapy. 1940: Normal child born in June.

embryology, Carnegie Institution of Washington, revealed "that, among the young human embryos already recorded in the literature, this specimen falls between the Kleinhans and the V. Mollendorf 'Sch.' Thus it occupies the third or at the most the fourth place, with its degree of trophoblastic differentiation and its estimated age of 11 to 12 days." Thus three months after x-ray therapy, the patient became pregnant for the first time in her life.

In spite of this accidental abortion the patient continued to menstruate regularly. No further treatment was given. Finally, in April, 1937, nine months after the small dose x-ray therapy, she became pregnant again. During the first two months of this pregnancy, the patient had pelvic discomfort and occasional spotting. She was given injections of progestin (Proluton) and calcium and wheat germ oil for one month, because of threatened abortion, due possibly to lutein deficiency. She was finally delivered at full term of a normal female child in December, 1937.

The patient nursed the baby for five months, although supplementary feedings were given. Menstrual bleeding returned four months after delivery. It was normal and regular except for a missed period in July, 1938.

Following her menstrual period in October, 1938, there was a period of amenorrhea of eight months' duration. During this time two Friedman tests were negative for pregnancy. Another series of four consecutive weekly endometrial suction biopsies were taken on April 20 and 27, May 4 and 11, 1939. All of these showed the endometrium to be in proliferative phase. There was no evidence of any lutein activity. Thus the ovarian failure had returned in a more severe form and was now characterized by amenorrhea and absent luteinization.

Two days after the last endometrial biopsy, a second course of small dose x-ray therapy was given. From May 13, 1939, to May 19, 1939, a total dose of 80 r. (measured with scattering) was delivered in four treatments to each ovary and to the pituitary gland. There was no menstrual period in June, but there were normal periods commencing July 3, and Aug. 9, 1939. She then became pregnant. There was no menstrual period in September. There were two positive Friedman tests on October 5 and 10, 1939. On Oct. 24, 1939, the patient developed pelvic cramps and spotting. A diagnosis was made of threatened abortion, which could be interpreted as another manifestation of deficient progestin activity. She was therefore given fourteen injections of 5 mg. of proluton each, three times a week. After the second injection, the pelvic pains and spotting disappeared. Thereafter, although symptom-free, she was given 2 mg. of proluton twice weekly for four months. The pregnancy proceeded uneventfully and on June 8, 1940, the patient was delivered of a normal male child. She nursed this child for nine months. There was no menstrual period during this time, and for six months thereafter, up to September, 1941.

<center>DISCUSSION</center>

This case strongly suggests that small dose x-ray therapy can favorably affect sterility due to ovarian deficiency. In 1935, the patient's sterility was accompanied by irregular menses, possible estrogen deficiency (as evidenced by bio-assays), and faulty luteinization (as evi-

denced by endometrial biopsies). The first course of small dose x-ray therapy was followed by normal menses and two pregnancies within nine months. The first pregnancy was accidentally interrupted by a premenstrual endometrial biopsy which removed a twelve to fourteen day old embryo, which proved to be the third or at most the fourth earliest embryo in the history of medicine. The monthly cyclical bleeding was not thereby disturbed. The second pregnancy resulted in the delivery of a normal child at full term. In 1939, four years later, the clinical picture of ovarian deficiency returned in a more severe form, as evidenced by amenorrhea and absent luteinization. A second course of small dose x-ray therapy was followed by restoration of normal menses and a third pregnancy with delivery of a normal child.

This case further illustrates the fact that the successful response to therapy of an endocrine imbalance, when viewed over a period of many years may be only temporary. The organism, after responding favorably for a time, may revert to the original deficiency picture. In the above case this was not unexpected, because the endocrine deficiency was profound, as indicated by irregular menses ever since puberty, hypopituitary type of obesity, six-year duration of sterility, and faulty luteinization.

The possibility that the favorable result might have been coincidental is to a great extent eliminated because of the prompt response to each course of x-ray therapy.

The original designation of this type of therapy as ''x-ray stimulation'' has been discarded in favor of the noncommittal ''small dose x-ray therapy.'' It has not yet been established that small doses of x-rays will actually stimulate the ovaries. It is possible that this type of therapy can destroy some inhibitory factor.

Martius and Kroning[12] have shown that small amounts of roentgen irradiation (5 to 50 r. at the surface) can so damage the follicle apparatus of rats and mice as to produce appreciable variations from normal of the estrus cycle. Evidence of the possible existence of an inhibitory factor in the ovary, which could be neutralized by the irradiation is seen in the work of Stein and Cohen,[13] and Robinson,[14] who have successfully treated amenorrhea and sterility by removal of the cystic portions of both ovaries; and by one of us (M. F.) who has successfully treated several cases of dysmenorrhea and painful breast hyperplasia by unilateral roentgen irradiation of one cystic ovary with inhibitory doses of roentgen rays.

The evidence concerning possible damage to the unfertilized ovum with resultant injury to the offspring has been based chiefly on the effect of x-rays on the fruit fly (*Drosophila melanogaster*),[3-7, 15] and to a lesser extent the mouse and guinea pig.[8] The frequency with which difficulties are encountered in attempting to transpose the results of animal experiments to human beings is well known. This species difference to

which many biologic phenomena are subject is also observed in the field of radiation genetics.   Even should the human germ cells eventually be shown to be capable of producing mutation forms as a result of sub-lethal radiation damage, the statistical probability of a previously ir-radiated ovum ever resulting in a monstrosity, following fertilization, is so small as not to constitute a hazard.

The majority of sterile women who respond successfully to small-dose irradiation usually menstruate for a varying number of months before conceiving.   Thus, the ovum which eventually becomes fertilized may very likely have been quiescent and inactive within a primordial follicle during the actual exposure to radiation, and in this state, it would be relatively radioresistant at that particular time.

Therefore, in view of the fact that the inevitability of germ plasm damage to the *human* ovum from small-dose irradiation has not yet been demonstrated, one ought not at this time deny this effective type of treatment to a woman who ardently desires a child.   The possible theo-retical dangers should be explained to the patient and the final decision left to her.

CONCLUSIONS

1. Roentgen rays administered to the ovaries and pituitary gland in small doses are capable of correcting an ovarian dysfunction of a de-ficiency type accompanied by sterility.

2. A case is reported wherein two separate episodes of ovarian de-ficiency with sterility in the same patient were each successfully treated with roentgen rays.

3. Though a review of the experimental evidence based on lower animals suggests the possibility of harmful effects to the germ cells of small doses of radiation, there is as yet no evidence and small likeli-hood that small-dose x-ray therapy constitutes a real hazard to the human ovum.

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AN ANALYSIS OF LATE MORBIDITY IN ONE HUNDRED CASES OF PREGNANCY TOXEMIA

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REPORTS in the literature show that considerable vascular and/or renal morbidity may be found in toxemia patients at the time of follow-up examinations. Toxemia recurs in approximately 70 per cent of the cases. Early investigators attributed the late morbidity to nephritis, whereas contemporary investigators consider the morbidity the result of essential hypertension. The latter interpretation is substantiated by autopsy records[12, 26, 27] upon patients who have died from hypertension at long intervals, following toxemia of pregnancy. Renal function tests, urinalyses, and urine sediment examinations, at the time of late checkup studies, show that the incidence of significant renal damage is slight in comparison to the incidence of hypertension.

While obstetricians generally agree on the high percentage of late morbidity found in toxemia patients, there is no unity of opinion concerning the importance of the toxemic pregnancy in causing this late morbidity. Some believe toxemia does not injure a normal vascular and renal system, but most obstetricians apparently feel contrariwise. No definite proof for either assumption may be found in the analysis of our patients, but certain details seem worth mentioning which seem to favor the former assumption.

The method by which pregnancy toxemia may cause persistent hypertension has not been satisfactorily demonstrated. That the hypertension may be secondary to renal ischemia produced by vascular damage from toxemia is a plausible hypothesis; however, convincing proof of such vascular damage in these patients has not been given. A kidney lesion, specifically due to toxemia of pregnancy and also capable of producing hypertension, has not been recognized by pathologists. It is confusing to observe that thickening of the basement membrane of the glomerular capillaries, found by Bell[38] and others[26] in the kidneys of patients who have died from toxemia of pregnancy, is also to be noted in the kidneys of patients who have died from essential hypertension. One might speculate that there is more in common between toxemia of pregnancy and essential hypertension than is commonly believed. The significance of basement membrane thickening in glomerular capillaries to the cause of essential hypertension and toxemia of pregnancy is not clear since the

same lesion is found in the kidneys of patients who died of other causes[26] without a history of either of these hypertensive syndromes.

If the insult of a pregnancy toxemia to a normal vascular system can produce essential hypertension, it should be reflected in the hypertension in women as compared with men. Bell,[38] in a study of autopsies upon 11,826 men and 5,882 women, found that the percentage of men who died from the sequelae of hypertension was greater than that of women. Statements to the contrary appear in the literature, but no reliable statistics accompany them.

Reid and Teel[16] have published an observation which bears out the contention that much of the late vascular morbidity attributed to toxemia of pregnancy is due to unrecognized, antecedent vascular disease. Thus, they found normal blood pressures during the second trimester of pregnancy in a fairly large number of women known to have essential hypertension; such women when first seen by obstetricians during the second trimester of pregnancy would probably be considered normal and consequently when seen after parturition may be considered morbid as the result of the toxemia. Taking cognizance of this pitfall, Teel and Reid[32] suggested a classification of the late pregnancy toxemias whereby a reliable blood pressure recording and urine examination prior to, or in the first trimester of pregnancy, was necessary in order to distinguish pre-eclampsia from essential hypertension and nephritis. If these data were lacking, the case was considered unclassified. Using this precaution, they found that only 21 per cent of 235 patients with mild pre-eclampsia, and one of 49 patients with severe pre-eclampsia had hypertension at a late checkup examination following parturition. This is a much lower incidence of vascular morbidity than is usually reported. It is possible, that with a more complete evaluation of patients' vascular and renal systems prior to pregnancy, the morbidity which can be attributed to toxemia may be reduced even more. It would seem that any statement regarding late vascular and/or renal morbidity, following toxemia of pregnancy which does not include blood pressure recordings and urine findings before pregnancy or in the first trimester, should be considered pure speculation.

Dieckmann and Brown[17] observed a fall in blood pressure during pregnancy in a small number of women with essential hypertension but did not state whether it was limited to the second trimester. We have observed this occurrence, but in our somewhat limited experience, the fall in pressure has been known to occur as early as the first trimester.

Teel and Reid[32] attributed the fall in pressure which they observed during the second trimester of pregnancy in women with essential hypertension to a similar but unexplained phenomenon they had observed in pregnant women known to have normal blood pressures. Andross has carefully charted the blood pressure curves of 154 normal women who were observed in our ante-partum clinic from the early part

of the first trimester to parturition; these patients had all been seen prior to pregnancy in the University Hospital and normal blood pressure recordings were found at that time. Andross was unable to detect an appreciable fall in blood pressure in any substantial number of these patients in any one trimester.

CLASSIFICATION OF TOXEMIAS IN 100 PATIENTS WHO RETURNED FOR A LATE EXAMINATION

The toxemias studied by us were classified, as suggested by Teel and Reid, according to what was known of the patients' cardiovascular and renal systems prior to pregnancy or in the first trimester.

TABLE I

CLASSIFICATION	TOTAL NO. CASES	SEVERITY		
		MILD	MOD.	SEV.
Essential hypertension	9	1	4	4
Nephritis	2	1		1
Pre-Eclampsia	12	8	1	3
Unclassified nonconvulsive	71	21	23	27
Unclassified eclampsia	6	0	0	0
Total	100	31	28	35

The patients with essential hypertension were seen in the University Hospital during the first trimester or prior to pregnancy and at one or both times had blood pressure elevations (140/90 or higher), essentially normal urines, and negative histories for nephritis. The patients with nephritis were treated in our hospital for severe acute nephritis several years before their toxemias, and they had returned for checkup examinations prior to pregnancy and were cured so far as could be determined. The patients with pre-eclampsia were seen in our hospital during the first trimester or less than a year prior to pregnancy, and at one or both times had normal blood pressures, essentially normal urines, and negative histories for nephritis. The unclassified nonconvulsive toxemia patients were not seen in our hospital prior to pregnancy or in the first trimester. Hearsay data accompanying these patients to the hospital were lacking in details and verification; they were not sufficiently reliable to permit classification in this report. It is interesting that 52 of the 71 patients in this group had toxemia when they were first seen by us in the second or third trimester. Five of the 6 patients in the eclamptic group developed convulsions before being seen in our hospital. The other eclamptic patient had a mild toxemia when first seen by us in the last trimester of pregnancy; the convulsions developed post partum.

For the purpose of brevity, the details of the criteria used in grading the severity of our cases will not be discussed. It is sufficient to note that the majority of patients included in the severe grade had blood pressures of 160/110 or greater and large amounts of albumin in the

urine (3-plus to 4-plus); the majority of the patients in the moderate group had blood pressures of 160/110 or higher and little or no albumin in the urine; the patients in the mild group had blood pressures of less than 160/110 and slight degrees of albuminuria (less than 3-plus). The presence of marked symptoms, as headaches, etc., or the presence of considerable edema, or significant eye ground changes, accounted for the placing of some patients in a more advanced group than would be indicated by the blood pressure and albuminuria.

Treatment.—All patients were treated conservatively upon a salt free, neutral ash diet and fluids forced.* Patients with mild cases were sometimes permitted to go home but were asked to return for weekly or biweekly visits. Patients with moderate and severe cases were hospitalized until the termination of pregnancy. Interruption of pregnancy when necessary was carried out by the method thought to be best suited to the condition of the patient.

TABLE II. TIME INTERVAL BETWEEN PARTURITION OF TOXEMIC PREGNANCY AND THE CHECKUP EXAMINATION

TIME INTERVAL	1-2 YR.	2-5 YR.	5-10 YR.	10 PLUS YR.
No. Patients	38	35	21	6

TABLE III. INCIDENCE OF BLOOD PRESSURE ELEVATIONS, ENLARGED HEARTS, AND PERIPHERAL VASCULAR SCLEROSIS AT THE TIME OF LATE EXAMINATION

CLASSIFICATION OF TOXEMIA	BLOOD PRESSURE ELEVATION AT CHECKUP*			ENLARGED HEARTS	PERIPHERAL VASCULAR SCLEROSIS
	MILD EL.	MOD. EL.	SEV. EL.		
Essential hypertension	4	1	2	1	1
Nephritis	0	0	1	0	0
Pre-eclampsia	0	0	0	0	1
Unclassified nonconvulsive	7	7	12	8	13
Unclassified eclampsia	1	0	0	0	1
Total	12	8	15	9	16

*Mild blood pressure elevation 140-158/90-100
Moderate blood pressure elevation 160-180/100-110
Severe blood pressure elevation over 180/110

Thirty-five per cent of the 100 patients who returned had hypertension; 16 per cent had peripheral vascular sclerosis, and 9 per cent had cardiac enlargement. The peripheral vascular sclerosis was minimal except in 5 patients, all of whom had severe hypertension. All but 3 patients with minimal arteriosclerosis had some degree of hypertension which appeared to be the basis of this morbidity. All cardiac enlargements were the result of hypertension except for one case of rheumatic heart disease.

The Lashmet-Newburg thirty-six-hour renal concentration test was started by the patients at their homes and completed at the hospital

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*See R. R. de Alvarez, reference 39.

TABLE IV. ANALYSIS OF KIDNEY FUNCTION TESTS, URINALYSES, AND URINE SEDIMENT EXAMINATIONS AT THE LATE CHECKUP

CLASSIFICATION OF TOXEMIA	KIDNEY FUNCTION TESTS				URINALYSES		URINE SEDIMENTS		
	NO. TESTS	NOR-MAL	MIN. IMP.	MOD. IMP.	ALB.	SUGAR	W.B.C.	R.B.C.	CASTS
Essential hypertension	8	6	2	0	0	1	1	0	1
Nephritis	2	1	1	0	1	0	1	0	1
Pre-eclampsia	12	11	0	1	1	0	0	1	1
Unclassified nonconvulsive	64	51	12	1	6	1	0	4	4
Unclassified eclampsia	6	6	0	0	0	0	1	1	0
Total	92	75	15	2	8	2	3	6	7

where the last two specimens were obtained for analysis, sediment examination, and measurement of specific gravity. A specific gravity of 1.029 to 1.022 was considered indicative of minimal impairment and 1.022 to 1.016 moderate impairment. The heat and acetic acid test was used to detect albumin.

Due to the uncontrolled conditions of the concentration tests, those showing decreased concentrating ability cannot be accepted as positive evidence of renal impairment. Fortunately the patients cooperated eagerly, and we are able to show that 90 of the 92 patients whose tests could be used had normal, or no more than minimally impaired, concentrating ability. Ten of the 15 tests showing minimal impairment disclosed specific gravities of 1.027 to 1.028.

Albumin and casts were found in the urines of three patients. One of these patients gave a history of earlier nephritis; the other two had severe hypertension, no history of nephritis, and their urine findings were considered significant of renal involvement secondary to hypertension. In 9 patients, the urine had either an occasional granular cast or a faint trace of albumin, a finding of questionable significance in view of a normal concentration test in 8. Hypertension was found in 7 of this group and the possibility of mild secondary renal damage could not be excluded. None of this group had a history of nephritis.

TABLE V. RESULTS OF FUNDISCOPIC EXAMINATION OF THE EYES AT THE LATE CHECKUP

CLASSIFICATION OF TOXEMIA	FUNDI AT CHECKUP*					
	NO.	NORMAL	G1	G2	G3	G4
Essential hypertension	9	2	6	1	0	0
Nephritis	2	2	0	0	0	0
Pre-eclampsia	12	9	3	0	0	0
Unclassified nonconvulsive	68	47	18	3	0	1
Unclassified eclampsia	6	5	1	0	0	0
Total	97	65	28	4	0	1

*G1, eye grounds showed evidence of vascular sclerosis as manifested by vascular attenuation, increase in reflex stripe, tortuosity, and arteriovenous notching.

G2, eye grounds showed more evidence of hypertensive change, as manifested by localized areas of angiospasm.

G3, eye grounds showed edema.

G4, eye grounds showed hemorrhages and exudate.

A few red blood cells were found in the urines of 7 patients, but in no instance was there an accompanying albuminuria or cylindruria.

Although an occasional white blood cell was found in the urines of many patients, significant numbers were found in only three. These three patients had normal blood pressures, and at the time of their toxemia did not have white cells in their urines. No further investigation was carried out on this group.

The degree of vascular sclerosis in the 28 patients showing at fundiscopic examination *G1* changes was minimal; in some instances there was debate among the ophthalmologists as to its presence. Eighteen in this group as well as the 5 patients who showed more advanced changes in their eye grounds had hypertension. It, therefore, appeared that there was a definite relation between the eye ground morbidity and blood pressure.

TABLE VI. THE FUNDISCOPIC CHANGES AT THE LATE EXAMINATION IN COMPARISON WITH THOSE DURING TOXEMIA. (44 PATIENTS) THESE PATIENTS HAD SEVERELY ELEVATED BLOOD PRESSURES AT THE TIME OF THEIR TOXEMIAS

CLASSIFICATION OF FUNDI AT TIME OF TOXEMIA		CLASSIFICATION OF FUNDI AT CHECKUP*				
		NORMAL	G1	G2	G3	G4
Normal	2	2	0	0	0	0
G1	28	22	6	0	0	0
G2	2	2	0	0	0	0
G3	9	4	4	0	0	0
G4	3	1	1	1	0	1
Total	44	31	11	1	0	1

*G1, changes in the eye grounds during toxemia were due to angiospasm of a generalized nature producing a generalized attenuation without variation in caliber. G2, G3, G4, changes are the same as above (see Table V).

Eleven of the 13 patients with residual eye ground pathology had hypertension. The 31 patients with normal fundi at the checkup examination had normal or minimal elevations of blood pressure. Here again the relation between eye ground morbidity and hypertension was apparent.

SUMMARY

The chief morbidity to be found in toxemia patients at late postpartum examination is hypertensive disease.

The observation, published by Teel and Reid, concerning the fall in blood pressure which they observed during the second trimester in women with essential hypertension, makes it seem likely that much of the morbidity which the literature has attributed to toxemia may be due to antecedent, unrecognized vascular disease.

It is suggested that patients who do not have reliable vascular and renal estimations prior to the toxemic pregnancy be omitted from morbidity studies.

In our study there was no evidence of significant vascular or renal morbidity in patients known to be normal prior to their toxemic pregnancies.

This study was carried out with the cooperation of the following doctors and departments in the University Hospital: Harold Falls, Department of Ophthalmology; Fleming Barbour, Department of Ophthalmology; Ralph Cooper, Department of Medicine; Richard Lyons, Department of Medicine.

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The authors performed a thymectomy upon a 17-year-old girl, under local anesthesia. The three indications given for the surgery were marked ease of fatigue, generalized malaise, and a very dry skin. The removed operative specimen measured 11 cm. and weighed 25 Gm.

One year after the operation the patient is reported as vivacious, active, and capable of leading a normal life without unusual fatigue. The skin continues to be dry in type. A previous thymectomy was done by the authors, in 1938, upon a patient with myasthenia.

CLAIR E. FOLSOME.

BIOLOGIC ASSAY OF THE ESTROGENS IN PREGNANCY BLOOD

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THE present study deals with the estrogenic potency of human blood in the various weeks of normal pregnancy. The method used is the one originally described,[1] with the exception that the sodium sulfate blood powder was extracted not only with ether but also with 95 per cent ethanol.

A comparison of ether extracts, alcohol extracts, and combined ether and alcohol extracts on the same bloods was carried out on 20 different pregnancy bloods. An analysis of the tabulations in Table I tends to show that ether is a better solvent than alcohol for the estrogens of blood, and that alcohol and ether combined give a slightly better result than when ether alone is used.

Fifteen different pregnancy bloods were hydrolyzed and titered for comparison by the above method. This was done by adding sodium citrate (to prevent coagulation), distilled water, and concentrated hydrochloric acid to pH 2. The blood was then boiled for fifteen minutes in a reflux condenser, cooled, and made to pH 6 with 40 per cent sodium hydroxide. The water was evaporated from the blood on a water bath and the sludge treated as in the method originally described.[1] We found no increase in the estrogenic potency on hydrolyzing blood by this method over the ether and alcohol extracts of aliquot blood samples run directly into the sodium sulfate (Table II).

Ether alcohol extraction of sodium sulfated blood powder was the method of assay employed on 86 pregnancy bloods, covering the various weeks of pregnancy from the fifth to the fortieth weeks. The stage of pregnancy was calculated by determining the number of days from the last menstrual period, and adding ten days. In most cases we were limited to withdrawing 10 c.c. of blood. This accounts for the fact that only 63 of the bloods proved positive. In a majority of instances in the latter weeks, at which period the concentration is high, two or more castrated mice could be used for determining the smallest amount giving a positive estrous reaction (full cornification). Two hundred and eighty-two assays were carried out.

As can be seen from Fig. 1, the estrogen blood level remains approximately at the highest nonpregnant level until the seventeenth week is reached (from 25 to 35 mouse units per liter). From then on, a steady

TABLE I. COMPARISON OF METHODS OF EXTRACTION ON ASSAY OF BLOOD ESTROGENS

CASE	DURATION OF PREGNANCY, WEEKS	ETHER EXTRACTION		ALCOHOL EXTRACTION		ETHER-ALCOHOL EXTRACTION	
		C.C. OF BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING	C.C. OF BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING	C.C. OF BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING
4376	36	4 3 3 2 1	++++ ++++ – – –	5 5 4 4 3	++++ – – – –	2 2 1 1 1 .75 .75 .50	++++ ++++ ++++ ++++ – ++++ – –
4357	33	10 7.5 5 2.5	++++ ++++ ++++ –	10 7.5 5 2.5	++++ ++++ ++++ –	10 4 2 2 1 1	++++ ++++ ++++ ++++ ++++ ++
4397	27½	4 3 3 2.5 2 2	++++ ++++ ++++ – ++++– (Mouse died)	5 5 3	++++ – –	3 2.5 2 2 1	++++ – ++ – –
4354	17	10 5 3	++++ ++++ –	10 7.5 5 3	++++ – – –	10 7.5 5 2.5	++++ ++++ +++ sl.
4368	17	7.5 5 5 6	++++ ++– – –	7.5 7.5 5	– – –	7.5 5 4 3 2 1	++++ ++++ – – – –
4367	15½	12.5 10 7.5	– – –	12.5 10 7.5	– – –	10 9 7.5	– –++++ +++++
4422	15½					15 15	– –
4402	14½	20	++++	20	++++	20	++++
4390 II	11½					20	++++
4388	11	30	++++	30	–	30	++++
4396	9					20 10	– –
4360	8½	30	–	30	–	30	+++
4390	7¼					20	–
4353	7½	20 10	– –	20 10	– –	20 10	– –
4379	7	40	–	40	–		
4365	6½	40	–	40	–		
4378	6	40	–	40	–		
4391	6					20	–
4350	5	20 10	– –	20 10	– –	20 10	(Mouse died) –
4357	5	30	–	30	–	30	–

upward trend is noted which reaches its maximum at term (from 600 to 1,300 mouse units per liter).*

In a previous publication,[2] the excretion of combined and free estrogens in the urine during pregnancy was described. In this, a
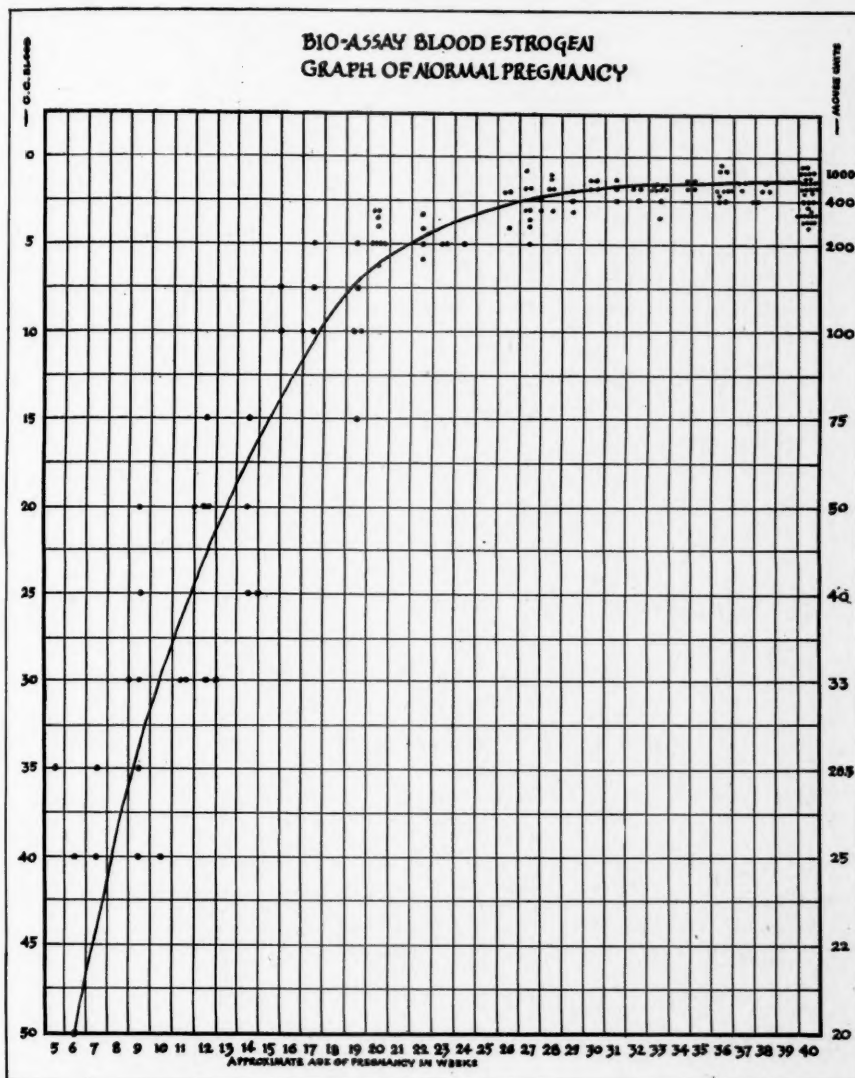

Fig. 1.

marked increase of the excretion of the combined estrogens was noted after the twenty-eighth week, and that of free estrogens after the thirty-second week. In the blood, the estrogens are probably in a free state,

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*Under conditions of assay in our laboratory a positive reaction is obtained with 0.08γ of estrone in contrast to 0.1γ which equals one international unit.

TABLE II. A COMPARISON OF ETHER-ALCOHOL EXTRACTS WITH HYDROLYZED CITRATED BLOOD EXTRACTS

CASE	DURATION OF PREGNANCY, WEEKS	ETHER-ALCOHOL EXTRACTION		SODIUM CITRATE HYD.	
		C.C. BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING	C.C. OF BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING
4602	40	2.2	+++	4	–
		2	++++	3	–
		2	++++	2	–
		1.8	++++	1.5	–
		1.5	–	1	–
		1	++++	1	–
		1	++++		
		1	–		
		1	–		
4603	40	3	++++	4	–
		2.5	++++	3	–
		2	++++	2.5	–
		1.5	++++	2	–
		1.5	–	1.5	–
		1	–	1	–
		1	–	1	–
		1	–		
4607	40	3	++++	2	++++
		2.5	++++	2	++++
		2.2	++++	1.5	++++
		2	–	1.2	++++
		2	–	1.2	–
		1.5	–	1	+++-
		1.2	–		
		1	–		
4621	40	3.5	+++-	4	–
		3.5	–	3.5	–
		3.2	++++	3.5	–
		3	++++	3.2	–
		5	–	3	–
		2.5	–	2.5	–
4643	40	3.5	++++	4	–
		3.5	++++	4	–
		3.25	+++	3.75	–
		3	++++	3.5	–
		3	++++	3.5	–
		2.5	–	3	–
		2.25	–		
4655	40	3.5	++++	4	–
		3	++++	4	–
		2.5	++++	3.5	–
		2.25	–	3	–
		2.25	–	3	–
		2	–	2.5	–
4626	40	2	++++	4	–
		1	++++	3	–
		1	++++	2	–
		1	–	1.5	–
				1	–
4803	17	10	+++	10	++++
		10	–	10	++++
		8	–	8	–
		7	–	7	–
		5	–	5	–

TABLE II—CONT'D

CASE	DURATION OF PREGNANCY, WEEKS	ETHER-ALCOHOL EXTRACTION		SODIUM CITRATE HYD.	
		C.C. BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING	C.C. OF BLOOD EQUIV. USED	MOUSE VAGINAL SMEAR READING
4724	13	30	++++	35	–
4672	12	20	++++	20	(Mouse died)
		10	–	10	–
4694	12	20	++++	20	–
		15	++++	15	–
4722	10½	35	–	35	–
4649	7	5	–	5	–
		4	–	4	–
		4	–	3.5	–
		3.5	–		
		3.5	–		
4720	7	35	++++	35	–
4769	5	35	++++	35	++++

because, as shown, the yield following hydrolysis was not increased. The small amount of estrogens found in the blood during the early weeks shows some parallelism with the small amount of free estrogens found in the urine at the beginning of pregnancy. In the urine the free fraction of the estrogens increases from 2 to 22 per cent of the total estrogens as the pregnancy advances to term. In the blood it rises from 20 units in the fifth week to 1,333 toward the end of pregnancy.

SUMMARY AND CONCLUSIONS

1. A biologic assay of the estrogens in 86 pregnancy bloods, covering from the fifth to the fortieth weeks, was performed.

2. Attempts to increase the yield by hydrolysis of the blood were unsuccessful.

3. Combined ether and alcohol extraction was found to be more efficacious than ether extraction or alcohol extraction alone.

4. A graphic presentation of the results of this study shows that the greatest amount of estrogens is present just before labor.

5. The estrogens in the blood increase slowly from the fifth week of pregnancy in each individual case; but not before the seventeenth week did any of the cases studied reach a level above the upper limit of estrogens in nonpregnant women.

6. From the seventeenth week of pregnancy progressive increase of estrogens in the blood takes place. Some parallelism of blood estrogen increase and free urinary estrogen increase appears to exist.

7. The estrogens in the blood probably circulate as free estrogens.

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THE LENGTH OF THE MENSTRUAL CYCLE

A STUDY OF 150 NORMAL WOMEN

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SINCE investigations during recent years have emphasized a definite time relationship between ovulation and menstruation, the length of the normal menstrual cycle has become more than a purely academic problem. It has long been taught that normally menstruating women do so at regular intervals. Expression of this view abounds in medical periodicals and even in modern textbooks. The general consensus of opinion is that twenty-eight days constitute the so-called "normal" cycle.

Kennedy (1937)[7] stated that of 10,000 cycles, 7,339 were twenty-eight days long, while 582 were twenty-one days long, and the rest were scattered over other days of the cycle. Nakagawa (1931)[9] writes that 97 per cent of a selected group of 2,000 women menstruated "regularly." Sanes (1916),[11] Hajek (1933),[6] and others report similar findings. Novak[10] quotes from the following workers who conclude that a majority of women have twenty-eight-day cycles: Kelly, 94.2 per cent; Kreiger, 70 per cent; Webster, Hart and Barboul, 71 per cent; Sanes, 72 per cent; and Meyer, 69.7 per cent. Novak in Curtis' *Textbook of Gynecology* stated that in most patients menstruation occurred at relatively regular intervals, and that the most common menstrual cycle was twenty-eight days long.

It is, however, self-evident that the ideal group for such studies would comprise women who, in addition to having some interest in or some good reason for keeping calendar records carefully, are at the same time normal from a gynecologic standpoint.

Studies of such individuals have been made in the past few years by Fluhmann,[4] Gunn,[5] and Allen.[1] Some of these records were kept by nurses and by college women whose age and manner of living might leave some doubt as to the normality of their menstrual behavior. However, according to the work of Arey[2] (1939), which our own findings confirm, occupation apparently does not alter the menstrual cycle significantly and may be disregarded in statistical studies. From analysis of 12,452 cycles which were actually recorded by 1,089 women and reported in papers published between 1889 and 1937, Arey also concluded that ordinary hospital records, oral testimony and similar data are unreliable.

The purpose of the present report is to make available information obtained from accurately recorded calendar data collected in the course

of consultations given to a group of 150 married women attending the Rhythm Department of the Fertility and Endocrine Clinic of the Free Hospital for Women. These women were mostly housewives; the majority were mothers in the third and fourth decades of life; they represented a composite of nationalities. No women were accepted for admission to this clinic who were not considered to menstruate normally. Retroversion, chronic cervicitis, and perineal lacerations and relaxations were the only pathologic entities recorded.

Upon admission to the clinic, the patient was given a calendar on which she was instructed to circle the date of the first day of flow each month. The calendar, marked accordingly, was returned to the clinic by the patient either in person or by mail within a few days after the onset of catamenia, in order that the "safe" and "unsafe" periods might be marked by a member of the clinic staff. Since these women realized the importance to themselves of accuracy and promptness in reporting the start of the menses, such a group would appear to constitute an ideal one for the statistical study of cycle lengths, the more so in view of the fact that their gynecologic condition was normal.

TABLE I. DISTRIBUTION OF CYCLE LENGTHS

DAYS	NO. OF CYCLES	DAYS	NO. OF CYCLES
10-14	2	31	175
15-19	10	32	90
20	10	33	61
21	11	34	46
22	35	35	36
23	57	36	15
24	108	37	8
25	204	38	7
26	296	39	5
27	357	40	2
28	369	41-45	6
29	286	46-50	4
30	206	51-100	4

TABLE II. ANALYSIS OF DATA

Nationality	American	Mean cycle length (days)	28.4
Occupation	Housewife	Average deviation of cycles from	
Number in group	150	group mean (days)	1.7
Age range (years)	19-42	Standard deviation of cycles from	
Mean age (years)	30.9	group mean (days)	2.2
Total number of cycles	2460	Occurrence of cycles equalling	
Range in number cycles reported	7-49	group mean (%)	15.0
Mean number cycles per person	16.4	Longer than group mean (%)	38.4
Shortest and longest cycle (days)	10-55	Shorter than group mean (%)	44.3
Modal cycle length (days)	28		

RESULTS

This group of 150 women was observed for a total of 2,460 cycles, the menstrual cycle being defined as the interval between recurrences of periodic physiologic uterine bleeding.

They ranged in age from 19 to 42 years with a mean of 30.9.

Per person, the number of cycles ranged from 7 to 49 with an average of 16.4 cycles.

The shortest and longest cycles were ten and fifty-five days, respectively. Each occurred once (Fig. 1).

The most frequent cycle was twenty-eight days long; this was observed in 369 cases only 15 per cent of the series (Table I).

The mean of all cycles was 28.4 days, and the average deviation from the group mean was 1.7 days. The standard deviation was 2.2 days; giving a standard range of cycle length of 25.2 to 30.6 days; 68.1 per cent of cycles fell within this range.
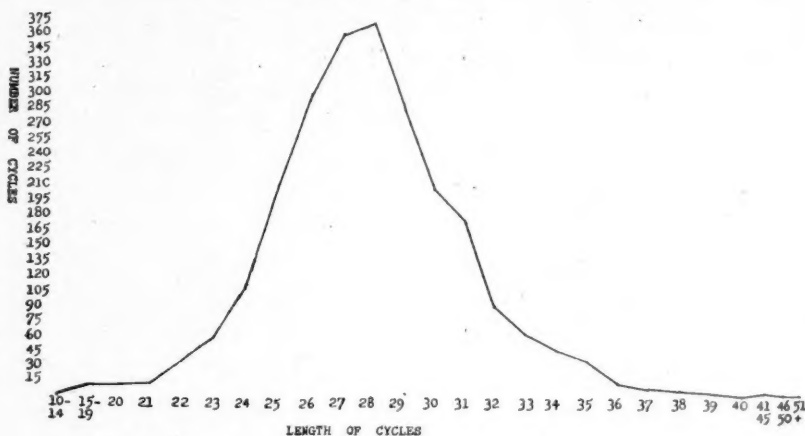
Fig. 1.

Thirty-eight and four-tenths per cent of the cycles were longer and 44.3 per cent were shorter than the group mean of 28.4 days (Table II).

It is noteworthy that of the entire group of 150 women only one showed a deviation of as little as ±1 from the mean of her cycle lengths. Of 7 cycles recorded by her, 5 cycles were twenty-seven days long; one was twenty-six and one was twenty-eight days. Such a low percentage of relatively regular catamenia clearly substantiates Fraenkel's well-known statement: "Das einzig Regelmässige an der Regel ist ihre Unregelmässigkeit" (the one regularity of the menstrual cycle is its irregularity).

SUMMARY AND CONCLUSIONS

1. An analysis of 2,460 calendar records of 150 normal women was made with the view of adding to the relatively few recorded observations on the human menstrual cycle. The cycle is defined as the interval between recurrences of periodic physiologic uterine bleeding.

2. The most common cycle was 28 days (which occurred in 15 per cent of cycles studied), and the average length of all cycles studied was 28.4 days.

3. There was no instance of absolute regularity in this series. The most regular cycles were in patients who reported the fewest. These would doubtless show more irregularity were a greater number of cycles reported.

4. There is no evidence of groupings in the multiples of 7; i.e., twenty-one-, twenty-eight-, or thirty-five-day cycles; nor do the cycles seem to fall into a few categories.

5. The distribution of cycle lengths follows the Gaussian curve.

6. This series again refutes the theory of the regularity of the human cycle, thus necessitating caution in judging the applicability and merits of the so-called "safe period" as a means of birth control.

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SPONTANEOUS PAINLESS PARTURITION IN A CASE OF PREGNANCY COMPLICATED BY TRANSVERSE MYELITIS*

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THE nerve control of the uterus has been the subject of study for many centuries. Our present knowledge concerning this nerve control is limited because of its multiple ramifications and because of technical difficulties in tracing its origin.

Roughly the nerve control can be divided into four divisions: (1) centers in the brain; (2) tracts in the spinal cord; (3) extrinsic connections with the spinal cord, and (4) intrinsic nerves in the uterus.

Centers in the Brain.—The centers in the brain are indefinite. It is believed at present that the highest center for uterine nerve control lies in the diencephalon. According to Kuntz,[1] diencephalic nuclei which are known to control autonomic function are located in the hypothalamus

and the wall of the third ventricle (Fig. 1, *B*). Which of these nuclei influence uterine muscular contraction is not known. In general, the descending pathways from these diencephalic autonomic centers involve

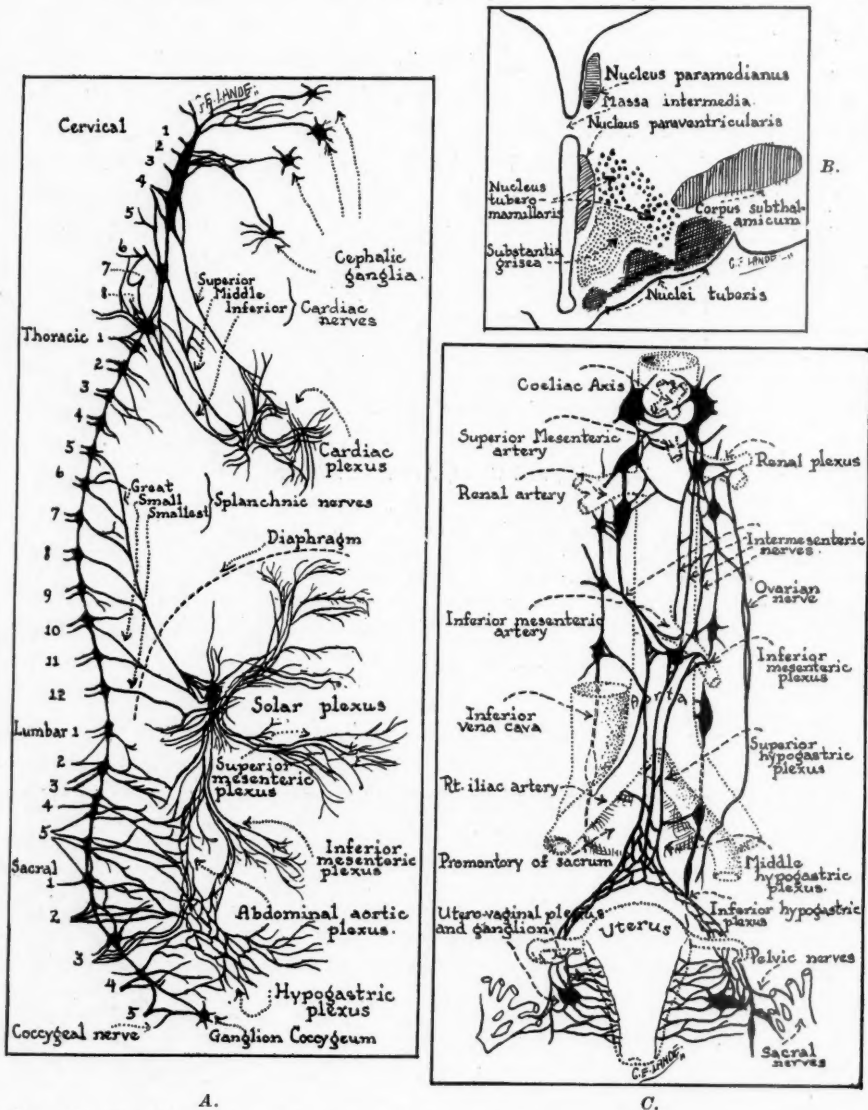*A.*   *C.*

Fig. 1.—*A*, Scheme showing general plan of the coarser portions of the sympathetic nervous system and its principal communications with the cerebrospinal system. (After Flower, modified by Morris.) *B*, Diagrammatic cross-section of the diencephalon showing relative positions of the diencephalic autonomic nuclei. (After Kuntz, modified.) *C*, Diagrammatic illustration showing the preaortic plexuses and the extrinsic nerve supply of the uterus. (After Dahl, modified.)

mainly the periventricular system to the tectal and dorsal tegmental region and from there, the tectobulbar and tectospinal tracts and dorsal longitudinal fasciculus, respectively.

Spinal Cord.—In the spinal cord, ganglia are located in the intermediolateral column of the dorsal and lumbar regions, from which fibers emerge through the lumbar spinal nerves and join the sympathetic trunk. From there they may go to form the sympathetic plexuses (Fig. 1, *A*). Their function is excitation of the uterine musculature. Other ganglia are located in the medioventral column in the sacral region, from which fibers go directly to the terminal ganglia through the sacral spinal nerves (Fig. 1, *A*). The function of the latter is supposed to be inhibition of uterine muscular contraction, but recently this function has been subject to question.

Extrinsic Spinal Cord Connections.—Connections between the spinal cord and the uterus are numerous. Fibers from the lateral branching inferior hypogastric plexus join fibers directly from the lower lumbar sympathetic trunk and the second, third, and fourth sacral nerves to form the uterovaginal plexus. The latter is located chiefly at irregular intervals along the attachment of the uterus and broad ligament (Fig. 1, *C*).

Intrinsic Uterine Nerves.—From the above-described plexuses, nerve fibers both myelinated and nonmyelinated penetrate all the uterine muscle layers but are not believed to penetrate the endometrium. Reynolds[2] believes that conduction of nerve impulses to and in the uterus proceeds by a succession of short synoptic pathways.

Normally parturition may be considered as a reflex act, the center of which is situated in the lumbar region of the spinal cord. Uterine function may, however, be independent of central nerve control. Numerous experiments by Reiman,[3] Rein, Goltz and Eward, Brachet, Kaminester and Reynolds,[4] Reynolds, Cannon and Rosenblueth[5] demonstrate this independence. Bach[6] believed that sympathectomy might interfere with parturition. Yaskin and Andrussier[7] quoting Schumann and Fist's case believed that lesions in the sacral region interfered with normal parturition but did not interfere with uterine contraction. Instances of spontaneous labor in cases of decentralized uterus are reported in the literature. The following case, which occurred in the wards of the Philadelphia General Hospital, services of Dr. Howell and of the late Dr. Frank Hammond, adds further evidence of this independence.

<div align="center">CASE REPORT</div>

H. O., a 37-year-old colored female, was admitted to the maternity ward Nov. 14, 1939, complaining of pain in the back, numbness of the legs and inability to walk. She stated that she was well until her last menstrual period which occurred Mar. 8, 1939. In November she developed urinary retention. Physical examination revealed an obese colored female lying in bed in apparent pain and unable to move her extremities. Eye ground examination revealed evidence of vascular sclerosis. Neck showed an enlarged thyroid. Heart was somewhat enlarged and forceful. Chest was normal. Blood pressure was 155/100. Left breast was normal. Right breast revealed two nodules, one in the left lower quadrant which was freely movable and the second in the left upper quadrant which was hard and irregular. Abdomen was enlarged to the size of a pregnancy at or near term.

Neurologic examination: Both pupils were equal but irregular in outline. Response to light and accommodation was prompt on the right, sluggish on the left. Corneal reflexes were normal. No facial or lingual

weaknesses were present. Abdominal reflexes could not be elicited. Complete flaccid paralysis of both lower limbs was present. A partial bilateral foot drop was evident. Patellar and ankle jerks were absent. Pain and thermic sensations were lost below the tenth thoracic nerve level as well as vibratory and position sense.

X-ray showed osteolytic metastases involving the twelfth thoracic and third and fifth lumbar vertebrae. A fetus almost at term was seen in breech presentation.
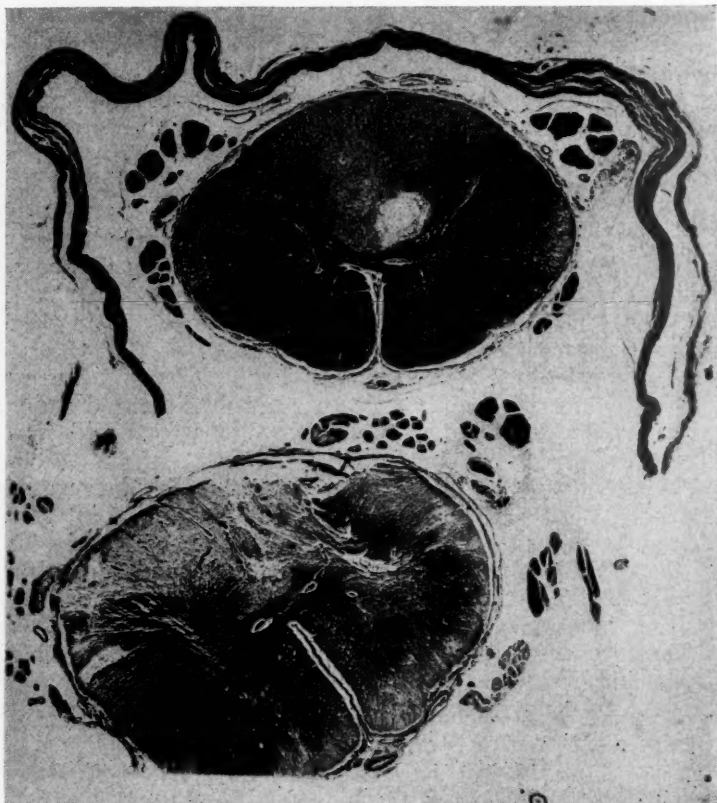

Fig. 2.—Cross section of the spinal cord showing myelomalacia of the lower thoracic segments and ascending secondary degeneration of the upper thoracic segment. Magnification 4×.

Laboratory tests: Urine contained five to ten leucocytes, 2 to 5 epithelial cells and was otherwise normal. Blood counts were normal. Blood Kahn test was negative. Nov. 26, 1939: 10 A.M.: The membranes ruptured spontaneously. Patient had no feeling of labor pain whatsoever. 12 noon: Fetal heart was 132 in upper right quadrant. 12:50 P.M.: A foot appeared through the vulva, then the second foot, followed by the buttock. The arms were decomposed. The shoulders were delivered, followed by the head. The baby breathed spontaneously. The patient was given intravenous ergotrate, gr. 1-320. The uterus contracted well. Very little bleeding was encountered. The baby weighed 6 pounds 8 ounces.

Placenta was delivered intact and weighed 1 pound 3 ounces. Histologic studies of the placenta revealed nothing suggestive of malignant epithelial cells.

The remarkable feature of the delivery was the total absence of pain. The patient was conscious of her experience only through sight. She felt nothing whatsoever.

Aside from some fever, the progress of the case was normal from an obstetric viewpoint. She was transferred to the cancer ward where a simple mastectomy was performed. They found (a) poorly differentiated adenocarcinoma and (b) multiple fibroadenomas. Patient recovered from the operative procedure; however, her general condition was fundamentally bad and she died April 8, 1940, more than four months after delivery.
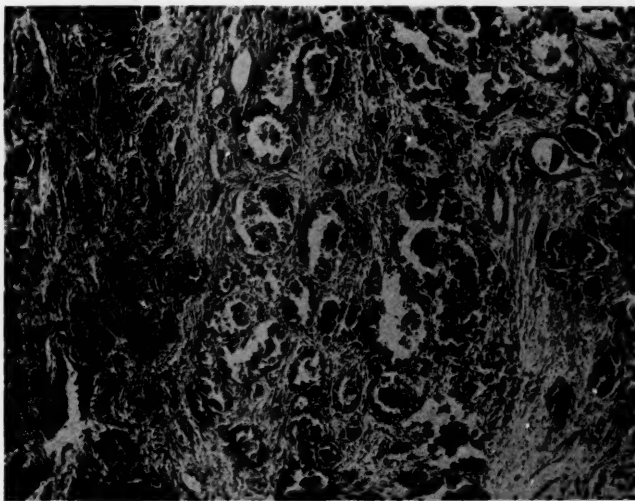

Fig. 3.—Cross section of the epidural tissue of the lower thoracic spinal cord segment showing metastatic adenocarcinoma. Magnification 92×.

Necropsy revealed the following outstanding features: Adenoma of the thyroid with hemorrhagic and cystic degeneration, mild coronary sclerosis and myocardial infarction, embolism in the left pulmonary artery, bilateral acute pyelonephritis, bilateral ureteritis and necrotic cystitis with calculi, thrombosis of the vena cava and left ovarian vein, chronic cholecystitis and cholelithiasis, metastatic adenocarcinoma of the twelfth thoracic and third lumbar vertebrae. The uterus was normal. Study of the spinal cord revealed carcinomatous involvement of the epidural tissue and dural veins. The cord showed almost complete myelomalacia in the lower thoracic region together with ascending secondary degeneration.

SUMMARY

The present knowledge of the nerve control of the uterus is reviewed.
A case is presented showing spontaneous painless parturition by decentralized uterus.

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COMPLETE INVERSION OF UTERUS LATE IN PUERPERIUM

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THIS is a report of a case of late inversion of the uterus recognized twenty-six days post partum. It suggests that the process may not always be the sudden dramatic and shocking condition usually described but one occurring gradually as a misdirected aberrant involution. This adds to the already increasing number of such cases and thereby indicates that the process is not as rare as was formerly thought and that its late occurrence during the puerperium should be considered.

It was of interest to note that the uterus even following removal could not be reduced by forceful manual effort. The mucosal aspect of the inverted organ gave the impression of soft roughening and furring.

The photograph of the cut specimen showed the ischemia of the myometrium which had developed and the beginning necrosis of the endometrium both of which would make the reposition of the organ undesirable even if possible. It is possible that natural or traumatic weakness of the lower uterine segment, which is supposedly relatively thicker and stronger than the fundus, may play a part. There was no indication noted, it was stated by the attendant, of dimpling, flattening, or undue bleeding immediately after delivery.

This episode suggests to me that there is a possible reason for retaining the word "late" to describe this insidious, formidable, yet seemingly rare, complication of the puerperium. It further indicates that the contour of the fundus should be noted for several days post partum, and that the character of any bleeding during this period be investigated not only for the possibility of partially retained placenta and subinvolution but also for inversion.

The incidence of 1:400,000 in the primiparas or 1:200,000 in multiparas, as reported by Zangemeister, would seem to represent only the cases in the literature prior to his review of the subject in 1933. I do not presume to indicate any probable ratio but suggest that uterine inversion may be an ever present possibility and one to be considered and anticipated along with other accidents of the third stage and the puerperium. Spontaneous inversion during the involution of the uterus is possibly explainable by congenital developmental defects in the complicated anatomic structure of the uterus itself, particularly in the lower uterine segment; and resorption of the musculature by a low placental implantation. Atony of the uterine wall would easily allow this process to ensue. "Partial atony of the uterine wall is no doubt an indispensable condition for the inversion of the puerperal uterus" (Bock). Low placentation with thinning out of the myometrium may have been a predisposing factor. Normally coordinated uterine contractions in an intact uterus would hardly tend to develop such an accident. If one visualizes the natural ingenious heavy inner circular musculature, the obliquely downward spiral course in three directions of the outer layer of muscles (Piersol), it would seem possible that this condition could only supervene if traumatic or absorptive disruption had occurred.

CASE REPORT

Mrs. R., aged 22 years, gravida i, was delivered at the Kingston Hospital by outlet forceps and episiotomy of a normal living child weighing 5 pounds 5½ ounces on Oct. 10, 1940, following a sixteen-hour labor. There was no undue hemorrhage at the time of delivery of the child, and the placenta was expelled intact twenty-four minutes later. A low-grade febrile course accompanied by intermittent spells of bleeding was interpreted as being due to an atonic and subinvoluted uterus. She was discharged on the seventeenth post-partum day. A blood transfusion of 500 c.c. was given during the puerperium as a general supportive measure. Questioning during the later puerperium at home elicited the story of continued slight bleeding, cramplike bearing-down pains, a sense of "dragging" in the hypogastrium and backache.

On November 4, twenty-five days post partum, this patient was readmitted to the Kingston Hospital with a completely inverted uterus. An unsuccessful attempt at manual reduction was made. The following day I was asked to see this patient in consultation.

On bimanual examination a spherical mass slightly larger than a baseball, though irregular and roughened, presented in the upper two-thirds of the vagina. No cervical rim could be found and the mass blended into the vaginal wall without any palpable interruption to the examining fingers. The left hand suprapubically through a relatively thin abdominal wall could feel no organ whatever, dimpled, flat, inverted or otherwise. The patient appeared ill and had a marked pallor. The pulse was thready, ill-sustained, and the rate was about 120. She had received 750 c.c. of citrated blood during the night and adequate doses of morphine. Hemorrhage had been only moderate since admission.

In view of the fact that reposition under deep anesthesia during the night plus the administration of epinephrine-hydrochloride (Daro) in an endeavor to relax the cervical sphincter had been unsuccessful, and since slight abdominal distention accompanied by a temperature of 102° F. had already developed, it was agreed upon that vaginal extirpation would be preferable. Blood count and hemoglobin determinations were 4,600,000 and 85 per cent, respectively, probably indicating increased capillary permeability and impending shock. Continuous and rapid administration of whole blood and plasma was begun. It was feared that a state of irreversible shock would soon develop. This was temporarily averted by the massive blood replacement, and in an hour it was felt that surgical treatment could be attempted.

Fig. 1.—Cut section of inverted uterus demonstrates hard irreducible consistency of the myometrium.

Under cyclopropane-ether anesthesia the uterus was withdrawn from the vagina en masse with surprising ease. Further attempt at reduction was obviously contraindicated due to the circulatory changes present. Introduction of a catheter showed that the lower portion of the bladder was drawn into the infunded uterus.

A vertical incision was made on the upper anterior surface of the prolapsed mass at the presumed level of the inverted bladder and down through the myometrium. The bladder was encountered immediately and with the index finger of the left hand was peeled upward and laterally thereby effecting satisfactory mobilization. The location of the ureters was obviously undeterminable. The tubes or ovaries were not drawn into the craterlike inversion. Double Kocher clamps were applied laterally at the same assumed level of and within the cervix, and a rapid removal of the herniated mass was effected with slight blood loss. The uterine arteries appeared thrombosed. Side-to-

side continuous hemostatic sutures were applied distal to the clamps and tight closure effected. There was notable absence of active bleeding during the procedure due to ischemia of the myometrium and the resultant degenerative change in the mural fibers. The mucous membrane of the vaginal vault was closed with a running stitch. The vagina was packed with iodoform gauze and a retention catheter placed in the bladder. The patient was returned to her room in fair condition. The immediate postoperative condition was relatively good. There was moderate shock treated by the usual measures and further transfusions. The response was good. Convalescence was uneventful though protracted. A low-grade septic course followed but with no definite pelvic peritonitis.

Examination on Jan. 15, 1941, revealed the vaginal vault well healed, the cervix small and unscarred, and the adnexa neither atrophic nor cystic.

SUMMARY

1. A case of complete inversion of the uterus recognized late in the puerperium is presented.

2. Ischemia and fixation of the tissue was sufficiently advanced to preclude reposition. The uterus could not be extraverted following removal.

3. The ovaries were not drawn into the crater, hence were not included in the extirpation.

4. The first step of the Spinelli procedure for replacement was utilized in mobilizing the bladder from the crater.

5. Low placentation with destructive effects on the lower myometrium is suggested by the given illustrations and offered as a possible contributory factor in the inversion.

6. Vaginal hysterectomy was necessary.

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CHRONIC PUERPERAL INVERSION OF THE UTERUS*

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PUERPERAL inversion of the uterus is quite infrequent but not so rare as is generally believed. When the inversion is present three to four weeks or longer, it is regarded by Bland and Goldstein to be chronic. The latter is by far the least frequently encountered. The following is the clinical history of such a case:

L. H., white, gravida i, aged 22 years, had an uneventful prenatal course. She was admitted on June 16, 1941, to the hospital where she was delivered. The first stage of labor of fourteen hours was uneventful, and the second stage of nineteen minutes was aided by 2 min. of pituitrin. A normal male baby weighing 7 pounds 10½ ounces was delivered by episiotomy and low forceps. The placenta was delivered thirteen minutes later by "modified Credé," and a blood loss of "400 c.c." followed. Ergotrate 2 c.c., pituitrin min. XIII, and 750 c.c. of saline hypodermoclysis were administered during the thirty-five minutes that followed the childbirth. A packing of 3 yards of gauze was also used to control the hemorrhage, and a 300 c.c. blood transfusion was given to the patient. Her condition was fair during the next twenty-four hours, but she had difficulty in voiding which persisted more or less until she was finally operated upon. On the fifth puerperal day, the episiotomy sutures began to slough, and a consultant was called to make a secondary repair. Her temperature had varied attaining a level of 101° to 103.4° F., and her pulse rate was 120 or higher. The consultant found a complete inversion to be present which had hitherto been unrecognized. The uterus could not be replaced, and he advised no further surgery until the patient's condition permitted. The patient received repeated transfusions, and sulfonamide therapy. The temperature gradually declined and was normal in about one week. She left the hospital by ambulance seventeen days after the delivery of her baby.

She had several hemorrhages at home and was admitted to the Cook County Hospital on July 26, 1941, forty days post partum with her vagina packed with gauze. The pack was removed in order to examine her and another was inserted. Her blood count showed hemoglobin 42 per cent, red blood count 2.55 and white blood count 4,500. In view of her poor condition, operative procedure was deferred until supportive measures, such as multiple blood transfusions, vitamin K, and an antianemic dietary regime were instituted. It was hoped that the uterus might involute further as the patient's condition improved. During the next seven days, the patient had 2 vaginal hemorrhages, and it was regarded unsafe to wait any longer. The second hemorrhage on the day preceding the operation was severe and necessitated a tight packing of the vagina, plus the injection of 500 c.c. of plasma, and 1,000 c.c. of citrated blood to improve her condition.

The patient was operated upon on Aug. 2, 1941. At this time the red blood count was 2.59 and hemoglobin 40 per cent. She was given a transfusion of 500 c.c. of blood during the operation, which was done under a light dose of spinal anesthesia reinforced by intravenous sodium pentothal. The uterus was considered to be too large for vaginal replacement by the Spinelli technique, therefore, the Haultain abdominal method was tentatively selected. Because of dense adhesions of the tubes and round ligaments to the peritoneal surfaces within the inverted pocket, it was necessary to incise the entire length of the uterus posteriorly in order to replace it. It was deemed wiser to remove this uterus, primarily because the edematous endometrium would necessitate much trimming and the uterus would then contain a sutured surface from cervix to fundus; secondarily, an infected uterus would be replaced into the peritoneal cavity of a patient whose resistance was certainly low; and finally, the hazard of such a scarred uterus for future gestation. A supracervical hysterectomy was easily done, and a Penrose drain was inserted into the dilated cervical ring. Four grams of sulfanilamide powder was placed into the pelvis.

The patient's postoperative course was stormy. On the fourth postoperative day the patient had a temperature rise to 105° F., and her pulse rate was 166. Thereafter, the temperature and pulse rate declined to normal. During the critical period of recovery the patient received several additional transfusions. She left the hospital on the sixteenth postoperative day, and when she was seen one month later, she had gained 10 pounds and appeared well.

The essential microscopic feature of this excised uterus was the replacement of the endometrium by a vascular granulation tissue.

PREGNANCY COMPLICATED BY ACUTE PERFORATED PEPTIC ULCER

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PEPTIC ulcer occurring with pregnancy is an exceedingly rare condition. Sandweiss, Saltzstein, and Farbman[1] found only one proved case of active peptic ulcer in 70,310 admissions of pregnant women to 5 Detroit hospitals during a ten-year period. In the same group of women numerous other gastrointestinal disorders, such as appendicitis, cholecystitis, and intestinal obstruction, were observed. These authors reported a case of a perforated ulcer in the anterior wall of the duodenum, occurring in a 42-year-old white woman (para x). The patient was in the sixth month of pregnancy when symptoms of extreme pain in the epigastrium and severe shock occurred. A differential clinical diagnosis of acute pancreatitis, perforated gastric ulcer, and ruptured gall bladder was advanced. The patient died shortly after delivery of a dead six months' fetus. The autopsy confirmed the diagnosis of a perforated duodenal ulcer.

Szenes[2] in a complete review of the European literature on the subject of peptic ulcer complicating pregnancy accepts only 3 cases in

which perforation of an ulcer or severe hemorrhage had occurred during pregnancy, or after delivery. The cases were confirmed by post-mortem examinations. One was in a woman (Chabannes' case[3]) in the fourth month of pregnancy in which perforation of a gastric ulcer occurred, also complicated by extensive tuberculosis of one kidney. A second case was that of Gminder[4] in a 23-year-old female (para iii) who developed peritonitis eight days following delivery and died on the twenty-third day following delivery. At the autopsy two chronic peptic ulcers were found on the anterior and posterior walls of the stomach. Gminder[4] felt that the ulcer on the anterior wall perforated during labor and the ulcer on the posterior surface perforated later following tremendous intake of fluid. The third case reviewed by Szenes[2] was that of Le Play,[5] occurring in a 27-year-old woman who died in the seventh month of pregnancy due to hemorrhage from a large ulcer on the lesser curvature of the stomach. Mulsou and Brown,[6] in 1936, described a case of fatal hemorrhage from a duodenal ulcer in a 41-year-old pregnant female. We wish to add another fatal case of acute perforated duodenal ulcer to the list of previously mentioned cases.

<div align="center">CASE REPORT</div>

Mrs. B. S., a 29-year-old, white, married female, entered the Buffalo General Hospital on Oct. 28, 1940, with the following complaints: On the day previous to admission to the hospital, after an uneventful full-term pregnancy, the patient delivered a normal male infant. Following delivery an average amount of bleeding occurred, and the patient rested comfortably for several hours, when she noticed a dull pain in her abdomen and a sense of fullness. She had a desire to ''move her bowels'' and took several enemas and some castor oil. This procedure was followed by nausea and emesis of black material. Her past history was not enlightening. Two previous pregnancies had been uneventful. There was no history of previous surgery.

Physical examination revealed a seriously ill white female, somewhat cyanotic about the lips and cheeks and markedly dehydrated. The temperature was 103.8° F., pulse 120, and respirations 36. Except for the rapid heart and respiratory rate, the examination of the chest and heart was not remarkable. Blood pressure was 100/80.

The abdomen was markedly distended, tympanitic and slight tenderness was present. No spasm or rebound tenderness was elicited. Peristalsis was absent. The uterus was in the normal post-partum state. Cervix was dilated and no tenderness could be found on pelvic examination. The lochia was normal. Laboratory examinations, including urine, blood counts, and blood chemistry, were all within normal limits. A white count on admission was 8,100 cells per c. mm. of blood and on the second day after admission was 5,600 cells per c. mm. of blood. A flat x-ray film of the abdomen showed several distended loops of small bowel lying on the right side of the abdomen. Gas shadows were not observed in the pelvic region and the loops visualized were separated, suggesting that the apparent obstruction might be the result of a peritonitis or ileus. The admission diagnoses varied, including paralytic ileus, puerperal fever with septicemia, appendicitis, and peritonitis.

On admission the patient was transfused with 500 c.c. of blood and duodenal decompression was instituted, with favorable results. On the second day after admission the cyanosis increased and oxygen therapy

was instituted. The patient became more distended and increasingly restless and irrational. A second 500 c.c. of blood was given with continuous intravenous fluids, but the patient died at 1:47 A.M., Oct. 31, 1940 (fifty-four hours after admission). A blood culture report after death was negative for growth of organisms.
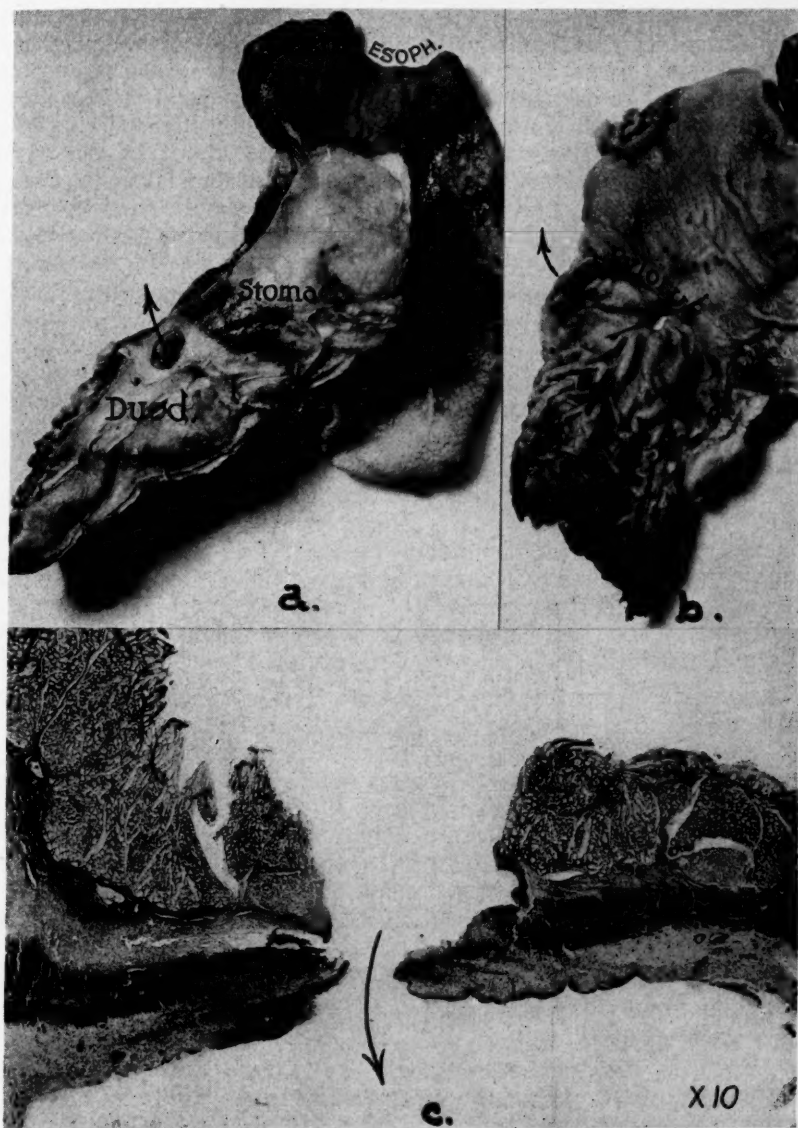

Fig. 1.—*a*, Anterior external view of the perforation of the acute duodenal ulcer. *b*, Illustrates a view of the mucosal surface of the stomach and duodenum. *c*, A cross section through the acute ulcer (stained with hematoxylin and eosin).

The autopsy was performed by Dr. Kornel Terplan and a summary of his findings follows:

"Markedly distended abdomen. A very large amount of fetid gas was found within the free peritoneal cavity. Diffuse fetid, serous,

purulent peritonitis, involving the entire peritoneal cavity and both subdiaphragmatic spaces, with at least 3 quarts of fetid, serous, dirty grey and slightly greenish fluid exudate, and with a pseudomembrane of about 2 mm. thickness completely covering all viscera in the peritoneal cavity, but especially the puerperal uterus and all the loops of small intestine which form a somewhat conglomerated mass. A perforated ulcus rotundum was found in the anterior wall of the first portion of the duodenum, measuring 1.1 cm. in diameter. There was complete disappearance of the original floor of the ulcer. A normal sized stomach, containing very little fluid, with scattered petechial hemorrhages in its mucosa and beginning post-mortal autolytic discoloration and superficial digestion were observed. Smears from the peritoneal cavity demonstrated a mixture of small gram positive cocci in short chains and many fusiform gram negative bacilli; also a few short gram negative bacilli, obviously of an anaerobic type.''

The chief diagnosis was perforated round ulcer in the anterior wall of the first portion of the duodenum with recent diffuse, fetid, serofibrinopurulent peritonitis. In addition, a recent serous pleuritis with atelectasis of both lungs and a partially noninvoluted puerperal uterus completed the autopsy findings.

The histologic findings of a section taken through the duodenal wall and the perforated ulcer are illustrated in Fig. 1. In both sides of the perforation the substance of the wall of the duodenum was almost completely destroyed. The borders showed very distinct effect of digestion and considerable inflammatory reaction. The absence of reactive changes in the duodenal mucosa in the area of the perforation was rather impressive. In the deeper areas of the submucosa, distinct evidence of inflammatory reaction, consisting of fibroblasts, lymphocytes, plasma cells, and relatively few leucocytes were found.

The muscle layers forming the border were covered by fibrinopurulent exudate. Inflammatory edema extended only for a short distance into the surrounding wall. The most marked inflammatory changes were seen in the subserosa with some extension into the outer serosal layer. The serosa was covered by a fibrinopurulent layer. There were autolytic changes within the muscle fibers bordering the perforation, accompanied by leucocytic infiltrates. A dense infiltration throughout the subserosa by plasma cells, fibroblasts, histiocytes, and a moderate amount of leucocytes was noticed. Capillaries were prominent and injected.

COMMENT

From the history in this case report, the perforation occurred a few hours after delivery. The patient developed peritonitis and died on the fourth day postpartum. Because of the more common gastrointestinal complaints of pregnant women following delivery, the possibility of peptic ulcer was not entertained as a possible diagnosis. Of course, as the symptoms of peritonitis appeared, the diagnosis of puerperal fever or a ruptured appendix was advanced. Numerous authors have called attention to the fact that peptic ulcer predominates in males, but even when peptic ulcer occurs in the female a beneficial effect of pregnancy on the symptoms of peptic ulcer has been observed. These beneficial effects have been observed by Roemheld,[7] Szenes,[2] Sandweiss, Saltzstein, and Farbman.[1] Szenes[2] thought that the lowered acidity of

the gastric juice, the deposits of fat about the stomach, and the change of position of the stomach which improved the circulation of the lesser curvature of the stomach were factors in promotion of healing of ulcers in pregnant females.

The most impressive finding in the case was the small size of the peptic ulcer and its apparent acute and recent state. These conclusions were formulated by the extensive acute, inflammatory reactions at both sides of the perforation and the complete absence of fibrosis or even actual granulation tissue along the walls of the perforation.

In summary, another case of acute perforated duodenal ulcer complicating pregnancy has been presented and added to the three previously described cases in the literature.

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CARCINOMA OF BARTHOLIN'S GLAND

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CARCINOMA of Bartholin's gland is considered so rare that it is usually recognized too late to be successfully treated, and the diagnosis is seldom suspected before surgical intervention. Only 38 cases[1] were collected in the latest reported tabulation. However, Cosbie[2] found one carcinoma of Bartholin's gland in 57 cases of carcinoma of the vulva and in Taussig's[3] series of 155 vulval cancers, 9 originated in the vulvovaginal gland. We report another case in which the condition was not suspected and which bore such striking resemblance to lymphogranuloma venereum that, regardless of repeated negative Frei tests, this remained as the clinical diagnosis.[4]

REPORT OF CASE

A negress, whose age was estimated at 65 years, was admitted on July 16, 1940, in a state of cardiac decompensation and mental cloudiness. The unsatisfactory history with reference to the vulval lesion was obtained from a daughter. Four years previously an abscess of the hip was incised and afterwards the process spread. One or two years prior to admission a sore appeared on the vulva. The physical examination and necropsy findings exhibited no relation between the vulval mass and a lesion of the hip.

Her terminal illness began one month ago with swelling of the lower extremities which was soon followed by edema of the hands and arms. Members of her family had noted indistinctness of speech and mental cloudiness for two weeks. The family history was negative for cancer. Venereal infection was denied. The patient had three daughters and one son, all in good health. The menopause occurred at an undetermined previous age.

Examination of the vulva revealed some edema of both labia majora, and pronounced enlargement of the left. The swelling on the left extended posteriorly to involve the buttock to the level of the coccyx. This tumorlike mass was irregularly ulcerated, and in the perineum there were several deep sinuses which discharged mucopus. Inguinal lymph nodes were not palpable. Intradermal tests with three different brands of Frei antigen were negative and no reaction followed the intradermal injection of chancroidal vaccine. The Wassermann and Kahn reactions on the blood were negative.

Fig. 1.

Generalized edema, weak heart sounds, and a low blood pressure indicated a terminal stage of congestive heart failure. Hemoglobin (Osgood-Haskins) measured 5.0 Gm. There were 3,900,000 red blood cells and 13,200 leucocytes per c.mm. of blood. The urine contained albumin, 2-plus. The patient did not respond to therapy directed toward the failing heart and died rather suddenly on the fourth day of hospitalization.

Necropsy confirmed the clinical impression of congestive heart failure. There was generalized arteriolar sclerosis. The heart weighed 445 Gm., and there were scattered areas of fibrosis in the myocardium. A large mural thrombus was attached to the apex of the right ventricle. Four small red infarcts were present in the right lung from embolic occlusion of the arteries and three of the large branches of the pulmonary artery on the right and two on the left were almost occluded by emboli. Subcutaneous edema was generalized. The peritoneal cavity contained about

1,000 c.c. of clear fluid, the right pleural cavity, 1,000 c.c., and the left 500 c.c. The pericardial cavity was distended with approximately 100 c.c. of clear fluid. Chronic passive congestion of lungs, liver, and spleen was evident. Incidentally, a small myoma was present in the anterior wall of the stomach, and in the mucosa of the duodenum there was a minute accessory pancreas.

The dorsal three-fourths of the left labium majus was enlarged and projected as a mass 18 cm. long and 9 cm. broad, which extended dorsally to the level of the coccyx. The surface was irregularly ulcerated and numerous sinus tracts discharged mucopus. On section the mass was composed of numerous locules filled with thick stringy mucus. The locules varied in size from minute ones to 1.5 cm. in diameter and were separated by delicate fibrous strands. There was no capsule. The inguinal nodes were not enlarged and on section no metastases were found.

Microscopically the newgrowth was composed of glands and locules which were generally lined with a single layer of columnar epithelium. All of the locules were filled with mucus, and in some the surface was denuded of epithelium, either in whole or in part, and from these, mucus had escaped into the interstitial tissue. The glands and locules were supported by narrow and broad bands of connective tissue. At the sites of ulceration leucocytic infiltration indicated infection (Fig. 1).

DISCUSSION

In an excellent review of the literature, Simendinger,[1] in 1939, was able to collect only 38 cases of primary carcinoma of Bartholin's gland. Of these 29 were adenocarcinomas and 9 were squamous cell carcinomas. The latter presumably arose from the duct. He stated that most authors agreed that metastases to the inguinal lymph nodes occurred early. Falls[5] and Strauss[6] mentioned that metastases were frequent and recurrence common, and Hunt and Powell[7] reported a poor prognosis in malignant disease of Bartholin's gland. However, Mayo and Barber[8] found that in their three patients, the tumors were of low-grade malignancy and that metastases occurred slowly. They attributed the unfavorable prognosis to uniform failure of early diagnosis. Lyle,[9] Falls[5] and Strauss[6] also commented on the fact that early diagnosis was seldom made and Rabinovitch[10] thought that the common source of failure of surgical procedure was the surgeon's inability to recognize at operation the malignant character of the neoplasm. Taussig[3] has aptly stated that "in no form of genital cancer do we find more evidence of inexcusable delay in seeking medical advice than in cancer of the vulva. This delay is only too often increased by failure in diagnosis or improper advice on the part of the family doctor."

The majority of cases occurred between 40 and 55 years of age. Simendinger[1] and Hoffmann[11] did not consider infection a predisposing factor. On the other hand Harer[12] thought that chronic inflammation (non-Neisserian) was probably a predisposing cause and observed that no cases had been reported in virgins. Falls[5] stated that chronic inflammation had been present in a considerable number of the reported cases, and in the case reported by Taussig,[13] the carcinoma followed trauma. In his later report[3] he found that infection was definitely present in 4 out of 9 Bartholin gland tumors.

Our case appeared to be of low-grade malignancy, and although the local tumor was far advanced, no metastases were found. It appears to us that various gradations as to rate of growth and the rapidity of metastasis would be present here as in carcinomas of other organs. This would depend on the degree of anaplasia. This case is also of interest because of the striking resemblance of the lesion to lymphogranuloma venereum. However, this resemblance is superficial and careful examination of the site should have indicated the differentiation. In the vulva the "elephantiasis" was confined only to one labium majus and did not involve the labium minus. It was also unilateral. These observations together with the repeated negative Frei test should have eliminated the possibility of lymphogranuloma venereum.

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RUPTURE OF THE SCAR OF A LOWER SEGMENT CESAREAN SECTION WITH TRANSVERSE INCISION

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IN RECENT years, obstetric interest has become more and more focused on the lower segment two-flap cesarean section with a transverse incision. The transverse incision has been known for many years especially through the work of Kerr, but has become more popularized lately by Marshall[1] in England and Phaneuf[2] in the United States. The arguments for and against the use of the transverse incision have been excellently discussed in Marshall's book on the subject.

One of the chief fears of obstetricians with regard to the transverse incision seems to be that of rupture. Nevertheless a perusal of the literature reveals only one reported case of rupture of the scar of a transverse incision in a subsequent labor. This was reported by Sheldon[3] from Irving's clinic. In addition Irving[4] has four other similar cases as yet unreported. These same five cases are also mentioned in Marshall's book. Unfortunately, due to lack of published statistics, there is no way of arriving at the incidence of rupture of the uterus following this technique. However, the fact that only five cases can be dis-

covered of rupture of the scar of the transverse incision would seem to indicate that the danger is minimal.

For the past four years the obstetrical service at Cumberland Hospital has adopted the use of the transverse incision as the procedure of choice. During this time, 46 such operations have been performed. Recently we encountered a case of spontaneous rupture of the scar of the transverse incision in one of our own cases. This we are reporting in detail.

CASE REPORT

I. R., aged 24 years, colored, gravida ii, para i, was admitted to the Cumberland Hospital, Dec. 24, 1939, on the service of Dr. A. E. Dunbar, complaining of weak labor pains of one and one-half hours' duration. Her expected date of confinement was Dec. 12, 1939. She had previously been delivered on Nov. 11, 1938, by a lower segment cesarean section with transverse incision for cephalopelvic disproportion following a thirty-six-hour labor with intact membranes. Her post-partum course was complicated by an endometritis of six days' duration. The patient also had been receiving antisyphilitic therapy.

Examination on admission disclosed the abdomen soft, fundus to be at term, fetus in the L.O.A. position, and the fetal heart of good quality in the left lower quadrant. Rectal and vaginal examinations were not done. Pains began about one hour before admission, continued every ten minutes, and were moderately strong. The membranes were apparently intact.

The patient was immediately prepared and taken to the operating room. Under local infiltration of 1 per cent procaine, a lower segment two-flap cesarean section with transverse incision was performed with delivery of a living male child. The placenta was removed manually.

Examination of the uterus preparatory to suturing the transverse incision revealed a second transverse opening into the uterine cavity about one and one-fourth inches below the new uterine incision. There was no evidence of bleeding from the edges of this opening which showed a firm glistening surface. Because of the absence of hemorrhage and the apparent scarification of the lower end, the opening was interpreted as a spontaneous rupture of the old transverse incision. Due to the difficulty of re-suturing the laceration, a hysterectomy was done. The uterus was amputated at the level of the site of the apparent rupture. The operating time was one hour and thirty minutes. General anesthesia of nitrous oxide and oxygen was given at the time hysterectomy was decided upon. The postoperative course was entirely uneventful and mother and child were discharged in good condition on the fourteenth day post partum.

Pathologic Report by Dr. S. Polayes.—Microscopic examination of sections through the anterior wall in the line of amputation showed the endometrium to be composed of decidual cells. The myometrium was partially replaced by scar tissue and contained areas of old hemorrhage. The sections corresponding to the recent incision showed no scarification and a few areas of fresh hemorrhage.

DISCUSSION

An interesting feature of this case was the absence of any symptoms or signs of rupture of the uterus. Because of the operative findings and

the pathologic report, we feel warranted in drawing the conclusion that the rupture was spontaneous and occurred before labor began.

Further study seems to indicate that the post-partum febrile course following the original section was the underlying factor responsible for the improper healing of the lower segment scar and its subsequent spontaneous rupture. Undoubtedly, too, the concurrent syphilis played a part. It is the experience of obstetricians in general that post-partum infection following cesarean section by any technique is the chief etiologic factor in subsequent rupture of the scar.

Experience has shown that supracervical hysterectomy is the procedure of choice in the treatment of rupture of a scar following section. The uneventful post-partum course of the case presented is in keeping with this.

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PROLAPSUS UTERI ASSOCIATED WITH SPINA BIFIDA AND CLUBFEET IN NEWBORN INFANTS

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IN 1927 Noyes[1] reported a case of uterine prolapse associated with spina bifida in the newborn infant. He also reviewed the literature up to that date and found 24 similar cases, each of which he abstracted. Most of the babies died within the first month after birth. Noyes' conclusions are as follows: "A review of the cases reported leads one to infer that the spina bifida is the primary etiologic factor in the occurrence of the prolapse. It would appear that if certain of the sacral nerves are drawn into the spina bifida, there is a partial or complete paralysis of the musculature of the pelvic floor resulting in secondary atrophy.

"On account of the high mortality in cases of spina bifida aperta, uterine prolapse associated with this condition is of little practical interest, but, inasmuch as present methods of diagnosis prove that spina bifida occulta is much more frequent than was previously suspected, a thorough search for this condition in all cases of uterine prolapse in which the etiology is not evident may throw some light on the subject.

"Ebeler and Duncker state that a study of 28 cases of uterine prolapse showed spina bifida occulta in 28 per cent, whereas an equal number of women without prolapse showed the condition in only 10 per cent. Further investigation of this interesting phase of the subject would seem to be warranted."

Ten years previously Palmer Findley,[2] writing on prolapse of the uterus in nulliparous women, had stated that in such cases it occurred most frequently in the newborn infant and in most of these instances was associated with congenital defects, notably spina bifida. He noted that the uterine prolapse was rarely evident at the time of birth, but developed during the first week. Such was the condition in the case reported in this paper.

From the literature, Findley found numerous associated lesions in the newborn cases, i.e., hydrocephalus, ankle clonus, clubfeet, scoliosis, kyphosis, flat or perpendicular pelvis, infantile uterus, flat and shallow vagina, elongated cervix, prolapse of rectum, inguinal hernia, paresis of perineal muscles and disturbed sensation in the lower extremities.

Fig. 1.—Showing infant with spina bifida tumor and prolapsed cervix.

Not all cases of spina bifida in the female infant are associated with prolapse of the uterus. Coughlin[3] reported operations upon 12 infants, of whom 7 were females, in none of whom was there prolapse of the uterus, although bowel and bladder paralysis were frequently noted and in some cases there were clubfeet.

Uterine prolapse occurring later in life in the nullipara may be associated with occult spina bifida. If it comes early, the association is more common.

Pollock[4] reported cervical and vaginal prolapse in a negro prostitute, 13 years of age, and this was not associated with spina bifida occulta as shown by x-ray; but she did have scoliosis of the thoracic spine, protuberant abdomen, and genu valgum.

Brocq and Beclerc[5] reported the case of a 30-year-old woman in whom x-ray studies revealed bicornate uterus and spina bifida occulta of the fifth lumbar vertebra. Apparently there was no uterine prolapse.

Von Graff[6] found 2 of 4 nulliparous women with uterine prolapse to have spina bifida occulta when examined by x-ray, and a third one suspicious of such defect. Among nulliparous women with prolapse he found about one-half to be of the "asthenico-ptotic" constitutional type of individuals with congenital weakness and looseness of the mesodermal tissues. These may develop prolapse of the uterus, which is a hernia of the pelvic floor, under stimulus of recent labor.

Laws[7] studied 3 multiparas with early occurrence of prolapse after operation, and all three had definite spina bifida occulta. He, however, repeated Ebeler's study of 25 parous women with prolapsus uteri, and only one had spina bifida occulta.

CASE REPORT

Newborn, white female infant, rather cyanotic at birth, but well nourished and weighing 6 pounds and 3 ounces, was apparently normal, except for a spina bifida tumor over the lumbar region which consisted of a fleshy mass about 3 inches long and 1½ inches across and covered with some purulent exudate on the dorsal surface. In addition, the infant had bilateral talipes varus (Fig. 1). At the sixth day, it was first noted that "there is a protruding mass from the vagina about 1 inch in diameter with opening in the center shown to be the cervix." As the child progressed this mass receded into the vagina somewhat. The urethra and bowel tract were normal. Although by the nineteenth day the infant had taken nourishment well enough to weigh 7 pounds and 2 ounces, she had fever from 100° to 103° F. each day, probably due to infection of the surface of the raw spinal tumor. The infant had normal red blood count and normal hemoglobin and leucocytosis of 15,300. The urine was normal.

On the twenty-seventh day it aspirated some milk, and thereafter was cyanotic and probably developed pneumonia, causing its death on the twenty-ninth day. Post-mortem examination was refused.

The mother was a normal white primipara, aged 18 years, and the father was normal and aged 22. There was no history of congenital anomalies in either family.

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Five women diabetics of menopausal age were given 1 mg. of diethylstilbestrol four times daily for eight weeks. The changes noted were not greater than the normal variations in diabetes. The results were so consistently negative that even though the series was small it seemed significant.

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PREGNANCY COMPLICATED BY HODGKIN'S DISEASE

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HODGKIN'S disease and pregnancy form a rather unusual combination, a recent report by Kushner[1] stating that only three cases have been reported in the literature. Although Jemmell[2] reported only one case, he gives references to 13 reports in which further cases are mentioned. In most of the other instances, the Hodgkin's disease existed before the patients became pregnant, was chronic in type, and terminated fatally after rather long periods of time. The shortest time elapsing between delivery and death was one hundred ninety days. In the case here reported the pregnancy had progressed to approximately twenty-four weeks before the Hodgkin's disease asserted itself.

CASE REPORT

Mrs. A. M., a primigravida, aged 33 years, first consulted me on April 16, 1941. Her last menstrual period began on Jan. 15, 1941; the expected date of delivery, therefore, was Oct. 22, 1941. The past history was negative except for a long existing eczema of the skin of the entire body with itching. Physical examination, Kahn test, and urinalysis were all negative except for the finding of an early pregnancy.

The gestation progressed satisfactorily, and the patient's complaints were insignificant until Aug. 1, 1941, when she appeared for her regular prenatal visit, complaining of a swelling in the right inguinal region. This was found to be a chain of enlarged glands, each about the size of a hazelnut. No other glands in the body were found to be enlarged at that time, and there was no local lesion which could have been responsible for this adenopathy. A white blood count on that day revealed 11,000 leucocytes with a normal differential distribution and without eosinophilia.

Two weeks later the glands had doubled in size and there were small glands in the left inguinal region and in both axillae. The patient had developed a definite weakness. Two weeks later the condition appeared to be progressing further with the right inguinal glands again having doubled in size. Biopsy was advised.

On September 5, the patient was hospitalized and a biopsy performed by Dr. S. Perlow. Microscopic examination of the removed tissue revealed an early Hodgkin's lymphogranulomatosis (Dr. I. Davidsohn). By this time the patient had developed a severe cough and her general condition was becoming worse. Roentgenogram of the chest revealed no abnormalities. The pregnancy was developing normally. Roentgen ray treatment of the glands was advised, but owing to the proximity to the developing fetus, the dosage was necessarily small, and screening heavy.

In spite of this treatment the glands in the right inguinal region continued to enlarge. The size of this gland mass, the cough, the respiratory difficulty apparently aggravated by the growing pregnancy, and the progressive weakness made it impossible for the patient to move around, walk, or sleep. On September 30, she was re-admitted to the hospital with the right inguinal glands the size of two fists and a beginning edema of the vulva. Blood check-up showed 21,250 leucocytes, 5,410,000 erythrocytes, and 71.4 per cent hemoglobin. The patient was typed and suitable donors secured.

The edema of the vulva progressed so markedly and so rapidly that induction of labor was deemed inadvisable. At the same time emptying of the uterus was rather imperative for the comfort of the patient and in order that massive roentgen ray treatment could be begun.

On October 7, a low fundal cesarean section was performed under ethylene-oxygen anesthesia. A female infant weighing six pounds fourteen ounces was delivered. Thorough examination of the infant revealed no abnormalities. In the mother, chains of enlarged periaortic glands were palpated up to the diaphragm on both sides.

The postoperative course was uneventful and the vulvar edema rapidly subsided. Massive roentgen ray therapy was begun as soon as it was felt that the wound was sufficiently healed. The condition of the patient became progressively worse, with elevation of temperature and no decrease in the size of the glands. Death occurred on November 22, forty-five days after the delivery of the baby.

Autopsy confirmed the pathologic diagnosis of Hodgkin's disease.

Extensive comment is omitted here because the many unusual features presented by this case are worthy of a more detailed study and report which will be made subsequently.

It might be well to summarize the more interesting features noted in the study of this case:

1. The apparent onset of Hodgkin's disease during the second trimester of pregnancy.

2. The rapidity with which the disease proved fatal.

3. The manner in which the pregnancy and apparently the baby were entirely unaffected by the Hodgkin's disease.

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TREATMENT OF CERVICITIS WITH NEGATAN (NEGATOL)

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ONE of the problems that confront a gynecologic clinic is the treatment of cervicitis. Cauterization of the cervix can successfully cure most cases. However, there are times when cauterization is either contraindicated or not available. As a substitute, the topical application of chemicals to the cervix in the treatment of cervicitis has led to such disappointing results that such therapy has virtually been suspended in the gynecologic clinic at Bellevue Hospital.

However, during the year 1938 a new preparation, Negatan (Negatol), was employed in the gynecologic clinic at Bellevue Hospital. As a result of a preliminary survey done during that year, it was concluded that the drug had shown such merit that it warranted further and more intensive investigation. Simultaneously with the clinical studies, K. K. Chen, of the Research Laboratories of Eli Lilly Corporation was determining the chemical and pharmacologic nature of the drug.

With the permission of Dr. Chen, his statements are quoted:

"Negatol is the condensation product of *m* cresol sulfonic acid and formaldehyde diluted with sufficient water to give a specific gravity of 1.17 to 1.18. This constitutes a 100 per cent strength. For experimental purposes dilutions can be made from it by volume. It is brown-black in color, and is definitely acid to litmus. A 10 per cent solution measures a pH value closely equivalent to that of N/10 solution of hydrochloric acid. It has an empyreumatic odor not unlike that of cresol. It possesses a strong coagulant action, precipitating dilute solutions of egg albumen and various alkaloids, such as ephedrine, atropine, strychnine, aconite, quinine and nicotine.

"Although Negatol is recommended for local application in gynecological practice, its toxicity has been determined in small animals by internal administration. The median lethal dose of a 10 per cent solution in mice by intravenous injection is 3.198±, 0.166 c.c. per kg. of body weight.

"Rats tolerate oral feeding of 0.4 c.c. of a 10 or 20 per cent solution of Negatol daily, except Saturday and Sundays, for a period of eight weeks. There is a slight inhibition of growth towards the end of the experiment. No pathological lesions can be demonstrated in the gastro-intestinal tract or parenchymatous organs.

"Local application of Negatol to rabbits' eyes or dogs' noses is followed by irritating effects.

"Repeated painting of higher concentrations (50 or 100 per cent) of Negatol on human skin occasionally results in a burning sensation, erythema, and superficial desquamation. It is, however, well borne by the majority of individuals.

"Repeated application of Negatol to dogs' vaginal walls and cervix, consisting of painting with a 10 or 20 per cent solution and insertion of a tampon saturated with 100 per cent Negatol, may be followed by congestion and excessive secretion if it is

made daily. When the medication is limited to twice a week, no pathological changes can be detected in the vaginal canal or cervix of uterus at the end of the eighth week. Only in one instance has a focal ulceration been observed.

"When injected intravenously in etherized cats, Negatol causes a fall of blood pressure with acceleration of respiration.

"No evidence has been obtained to show that Negatol is absorbed from mucous membranes, skin or extravascular tissues."

It is to be emphasized that the purpose of the present study is to evaluate the therapeutic efficacy of negatan in the treatment of cervicitis. No attempt was made in this investigation to compare the effect of Negatan with other methods of treatment.

Cervicitis cases were classified into five groups, after the classification of H. B. Matthews:*

Class 1: Superficial erosion of recent duration.
Class 2: More extensive erosion of longer duration.
Class 3: Extensive erosion of long duration.
Class 4: Extensive erosion with eversion, laceration, and Nabothian cysts.
Class 5: Limited to endocervicitis alone.

Obviously, even such a classification has its drawbacks because of individual interpretation. Each doctor, on examining a patient, was asked to draw on a specially mimeographed chart the extent of the erosion.

The following outline describes the method of treatment:

Patients with cervicitis returned twice a week for treatment, at which time the vagina was cleansed, the cervical erosion was painted with 100 per cent negatan, and a gauze wick, the proximal portion of which was dipped in 100 per cent negatan, was placed in the cervical canal. The wick was held in place by a dry, vaginal tampon which was removed in twenty-four hours and followed by a cleansing vinegar douche. It must be stated that frequently patients did not return as often as twice a week for treatment, sometimes as long as one or two months elapsing between treatments. However, in the statistical compilation on the duration of treatment, there was no way of correcting for the factor of irregularity of visits.

The results obtained in the treatment of cervicitis are shown in Table I.

TABLE I

CLASS	CURED	DURATION NO. DAYS	AVE. NO. TREATMENT	IMPROVED	DURATION NO. DAYS	AVE. NO. TREATMENT	FAILURE	AVE. DURATION NO. DAYS	AVE. NO. TREATMENT
1	43	35	5.0	6	32	4.5	2		
2	67	48	6.0	32	35	4.0	1		
3	35	61	9.5	29	58	6.1	5	59	8
4	10	79	9.7	11	43	5.0	2		
5	14	41	5.5	0	0	0	3		
	169 (65%)			78 (30%)			13 (5%)		

Total number of cases, 260

*Am. J. Surgery 26: 233, 1937.

Cases were termed "improved cases" if a study of the drawings revealed a considerable lessening of the extent of erosion. Even if the "improved cases" were placed in the "failure" column; because an ultimate cure had not been obtained, a 65 per cent cure of cervicitis by the topical application of a chemical to the cervix is most impressive. It is apparent from Table I that the more severe the erosion, the more treatments it required, and the longer time it took to effect a cure. In none of the patients treated were there any untoward reactions. It was noted during the course of our investigation that negatan could be effectively used as a hemostatic agent. Consequently, it found use in post-cautery bleeding of the cervix, traumatic bleeding of the cervix as tenaculum puncture wounds following a tubal insufflation, and even in those cases of moderately profuse bleeding from cancerous lesions of the cervix.

In conclusion, an evaluation of the results obtained in the treatment of 260 cases of cervicitis with this preparation permits us to recommend its use in those cases of cervicitis where cauterization is either contra-indicated or too hazardous a procedure.

Albert, M.: Massive Adrenal Carcinoma With Pseudohermaphroditism, Brit. M. J. 2: 265, 1941.

The author reports the case history of a two-year-old female infant with an adrenal cortical carcinoma. The child's mother complained of the infant's fretfulness and abdominal swelling over a two-week period. Physical examination revealed a thin puny infant showing axillary and pubic hair growth of male distribution. The clitoris was enlarged with a small glans. Rudiments of a prepuce were visible. An enormous ovoid, smooth, hard mass was palpable in the right abdomen, bulging the right flank outward from the costal margin to the iliac crest. The mass did not move on respiration. A diagnosis of massive adrenal cortical tumor with pseudohermaphroditism was made. Laparotomy revealed a right adrenal tumor 9 by 6 inches in diameter. Enlarged para-aortic glands were removed for section, and the abdomen closed. The child's general condition rapidly deteriorated and she died the following day.

Post-mortem examination revealed the left adrenal gland and kidneys to be normal. No evidence of metastases was found in the liver. The uterus was very small and the ovaries were small fibrotic nodules.

Histologically the report showed "a cellular malignant tumor with the character of a carcinoma of the suprarenal cortex. Details are more distinct in the gland specimen as the tumor itself is the site of extensive necrosis."

The article discusses briefly the alteration of sex characters by hormonal imbalance due to adrenal gland changes. Excessive cortical sterone in the female before the onset of female sex characters may result in pseudohermaphroditism and the onset of excessive hormone after puberty may result in adrenal virilism. In the male, excessive sterone may cause feminism.

FRED L. ADAIR AND WILLIAM ROSENBAUM.

Department of Book Reviews

CONDUCTED BY ROBERT T. FRANK, M.D., NEW YORK

Review of New Books

Gynecology

The ninth edition of the now classic textbook of **Diseases of Women**[1] by H. S. Crossen and R. J. Crossen has appeared. This edition continues to show improvement throughout in its presentation of the fundamentals of gynecology. All in all it is one of the most informative treatises for the practitioner, as well as for the specialist, because of its accuracy, the careful arrangement, and the concentrated presentation of facts. In spite of its being kept fully up-to-date, the increase in number of illustrations by sixty-nine, and the addition of a bibliography of twenty-three pages, the volume is fifty-one pages shorter than the previous edition. This difficult task has been accomplished by meticulous sifting and condensation. In this edition, special emphasis has been placed on the physiologic aspects of diseases.

R. T. FRANK.

Novak's **Gynecology and Female Endocrinology**[2] is designed primarily for the general practitioner and medical student. It covers both of these fields in a fairly exhaustive fashion, conforming in most ways to the usual standard textbooks. While diagnosis and treatment have been featured, all operative details have been purposely and wisely omitted. The text is concise and clear. The endocrine mechanism of menstruation and pregnancy is very well presented. The discussion of physiologic tumors of the ovary likewise deserves commendation for its clear-cut exposition.

A main feature is played by the abundant and exceptionally good illustrations. For gross illustrations, many are borrowed from classical sources, with due credit to the source; the microscopic illustrations are mainly from the collection of the author and are numerous, well chosen and most beautifully executed. In addition there are a number of handsome colored plates. Each chapter is concluded with a short, well-selected, useful bibliography.

Of the more than 600 pages, 445 are devoted to gynecology, the remainder to endocrinology. The present trend to overemphasize organotherapy, rather than endocrine diagnosis, is unconsciously evidenced by the fact that the chapters on endocrinology *begin* with "General Principles of Gynecological Organotherapy." The author shows a more marked trend toward conservative therapy in endocrinology than he has heretofore. He overemphasizes, in my opinion, the applicability and value of suction biopsy as may be seen from the following: Under the heading of "Occasional Therapeutic Value," he states that "As with ordinary curettage, functional bleeding may be cured by suction curettage." Nor can we agree with the statement that "It is probable that certain endometria are refractory to the growth

[1] **Diseases of Women.** By Harry Sturgeon Crossen, Professor Emeritus of Clinical Gynecology, Washington University School of Medicine, etc., and Robert James Crossen, Assistant Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine, etc. Ninth edition, entirely revised and reset. 948 pages with 1127 engravings, including 45 in color. The C. V. Mosby Company, St. Louis, 1941.

[2] **Gynecology and Female Endocrinology.** By Emil Novak, Associate in Gynecology, the Johns Hopkins Medical School, etc. 605 pages with 425 illustrations, many in color. Little, Brown and Company, Boston, 1941.

effects of estrogen. . . .'' The multiple subdivision of causes of both menorrhagia and amenorrhea appear hardly warranted in the present state of our knowledge. The chapter on sterility, which includes both the male and female, is excellent. It might have been wise to emphasize even more strongly that lipiodol hysterosalpingography must be limited to patients whose tubes have already been proved nonpatent by means of the insufflation test. The volume is concluded by a chapter on pregnancy conditions in gynecologic practice.

R. T. FRANK.

Obstetrics

A new monograph, **Preeclamptic and Eclamptic Toxemia of Pregnancy,**[3] by Lewis Dexter and Soma Weiss, analyzes this problem by a physiologic approach. The recent untimely death of Dr. Weiss is greatly lamented in the loss to American medicine of his brilliant mind.

Among the various clinical and pathologic phases investigated were edema, changes in arterial pressure and other factors of hemodynamics, and function of the kidneys. In discussing the findings of these investigations, the authors have sought to interpret recent literature in the light of their own results. By exclusion, a primary humoral etiology of generalized edema in pregnancy is suspected. No significant relationship between posterior pituitary and hypertension of late pregnancy could be adduced, nor could the toxic reactions of this pituitary be regarded as similar to toxemia of pregnancy. The authors were unable to determine the presence of a pressor substance (renin) in the placentas of hypertensive pregnant patients. A circulating pressor substance, if present in the mother, apparently does not cross the placenta to affect the infant similarly. Hormones were not found to produce a syndrome comparable to human toxemia in experimental animals, and pregnancy in animals evidently does not accentuate hypertension induced by renal ischemia.

In discussing the clinical and pathologic features of pre-eclampsia and eclampsia the authors have exhaustively studied 80 such cases with special reference to hypertension antedating pregnancy. The results of these clinical and laboratory studies again have been compared with a large group of similar studies in recent literature. The pathology of renal changes in eclampsia and infections and the degenerative lesions are well illustrated. There is an excellent section on cortical necrosis and another on vascular collapse in eclampsia. The various theories of etiology are carefully analyzed. The classification of the toxemias of pregnancy offered by the American Committee on Maternal Welfare is regarded as mildly unsatisfactory, at least, on grouping. The immediate renal lesion of eclampsia is regarded as a glomerulonephrosis. The authors feel that while no specific ''toxin'' has been found responsible the placenta must be regarded as the ''intrauterine factor'' responsible, although the pathogenesis is due to multiple rather than to single operative factors. They offer a diagrammatic representation of their conception of the factors involved. There is a significant suggestion that the relationship of isoimmunization and isoagglutinins has not been sufficiently studied.

The various methods of treatment are dissected, many are discarded, some are recommended. Aside from prenatal care and practice of preventive measures, reduction or prevention of edema, and of sodium retention in the tissues is regarded as the most important single principle involved.

This monograph will greatly interest not only the clinical obstetrician but as well the internist and the physiologist, one from the medical, the other from the research aspects presented.

PHILIP F. WILLIAMS.

[3]**Preeclamptic and Eclamptic Toxemia of Pregnancy.** By Lewis Dexter, M.D. Research Fellow in Medicine, Harvard Medical School, and Soma Weiss, M.D., Hersey Professor of the Theory and Practice of Physic, Harvard University, etc. In collaboration with Florence W. Haynes, Herbert S. Sise, and James V. Warren. 415 pages with 44 illustrations. Little, Brown and Co., Boston, 1941.

Dieckmann, an outstanding contributor for years to both the clinical and research aspects of the toxemias of pregnancy, offers a new monograph, **Toxemias of Pregnancy,**[4] on the subject. The book has been written with two objectives in mind: to acquaint the obstetrician with some of the recent contributions on physiology pertaining to obstetrics, and to acquaint the investigator, untrained in obstetrics, with some of the physiology and pathology of obstetrics.

.As to classification of the toxemias, the author discusses the grouping offered by the American Committee on Maternal Welfare. He feels that no case should remain unclassified, even if the diagnosis has to be changed at a later date. A study of the factors influencing incidence leads to the conclusion that high average temperature, small range of temperature, and high measure of rainfall are of importance. The section on Pathology brings together the contributions of Bell and Page, and others, on studies of the glomerulus.

The section on Normal and Abnormal Physiology covers a wide range of subjects. The author regards the decrease in blood and plasma volume in the eclampsias a finding which precedes the clinical symptoms, as an important factor. Attention is directed to factors which may initiate or intensify blood concentration. The position is taken that a hypoproteinemia does not cause the eclamptic conditions, nor the accompanying edema. The changes in many of the blood constituents seen in eclampsia, blood sugar, uric acid, and so forth, are regarded as a result and not as a cause.

There is an extended consideration of blood pressure. Hypertension due to narrowing of the arterioles may be on an angiogenic basis (pressor substance) or neurogenic (stimulation of vasomotor centers). Dieckmann feels that the reaction from injection of pituitrin into patients with toxemia is an aid in distinguishing between preeclampsia and other hypertensive diseases. Patients with essential hypertension gave the most marked response to the cold pressor test. Urea clearance is considered as of little value in differential diagnosis. Dieckmann disregards the placenta or its changes as a cause of toxemia, and does not feel hormonal studies in toxemias have been carried on long enough to determine their significance. The high value of ophthalmic examinations is stressed. After evaluating the physicochemical changes in the pregnant woman he summarizes those regarded as of etiologic importance.

In the section describing the clinical aspects of the toxemias of pregnancy, hypertensive disease of pregnancy, and acute and chronic disease of the kidney are included. One finds a full discussion of renal ischemia, renin, and the mechanism of edema. The treatment of eclampsia includes a consideration not only of pharmacodynamics but a review of various treatments proposed by individuals or hospital. Very definite criteria are set for the termination of pregnancy. The final section of the book considers, statistically, the maternal mortality, the problems of the fetus in toxemic pregnancy. In considering the sequelae, Dieckmann does not believe that true eclampsia or pre-eclampsia results in permanent disease of the vascular or renal systems.

This volume is a splendid exposition of all phases of this most important problem in obstetrics, and the reviewer feels the objectives have been fully attained.

PHILIP F. WILLIAMS.

This manual on **Clinical Roentgenology of Pregnancy**[5] is presented by Dr. Snow to illustrate the methods which he has been using successfully on his hospital services. There is a critical analysis and interpretation of various techniques, and Dr. Snow

[4]**The Toxemias of Pregnancy.** By William J. Dieckmann, Associate Professor of Obstetrics and Gynecology, University of Chicago, etc. 521 pages, with 50 text illustrations and three color plates. The C. V. Mosby Company, St. Louis, 1941.

[5]**Clinical Roentgenology of Pregnancy.** By William Snow, Director of Radiology, Bronx Hospital, Roentgenologist-in-Charge, Harlem Hospital, New York City. 178 pages with 117 illustrations. Charles C Thomas, Springfield, Illinois, 1942.

offers concisely the methods which he has found of greatest value. The technique is well illustrated, and the mathematics of the subject have been simplified as far as possible. There is a very timely discussion on the midpelvis, the importance of which has sometimes been overlooked in the anxiety regarding the amplitude of the inlet. The clinical problems of the fetus have been well handled. There is an excellent discussion regarding the soft-tissue technique and the localization of the placenta. Of particular value in this book is the well-illustrated series of case reports of unusual situations which Dr. Snow encountered. The illustrations are unusually clear. This manual should be of interest and of value to both the obstetrician and the roentgenologist.

PHILIP F. WILLIAMS.

In his **Contribution to the Study of Abdominal Pregnancy**,[6] a brief thesis, Orta Menendez presents a well-balanced consideration of the subject with special emphasis on the diagnostic procedures to be followed when abdominal pregnancy is suspected. Most of his techniques are followed in this country although few would attempt to estimate the status of the uterine cavity by passing a very fine bougie (Douay-Broca maneuver). An extensive bibliography is appended.

R. J. WEISSMAN.

The minutiae of the essential features of the puerperal course of over 1,000 women, representing a great amount of careful work, were studied statistically by Ruelas in his thesis **Observations on the Clinical Course of the Puerperium.**[7] Conclusions of interest include Ruelas' finding of more rapid involution and decreased incidence of afterpains in women of "hypergonadic biotype." The author recommends having the mother sit up in bed on the first post-partum day, up in a chair the second or third day, and ambulant by the fourth day. This procedure favors free drainage of lochia and normal bladder and bowel function. The literature is freely and extensively quoted.

R. J. WEISSMAN.

An interesting monograph, **Semiology of the Ovary,**[8] presents Rodrigues' review of ovarian physiology, histology, and endocrinology. Most impressive are the excellent studies of vaginal smears (Shorr method), as a mirror of ovarian endocrine activity. Many of the plates are in color and full details of many staining techniques are given.

R. J. WEISSMAN.

The Second Edition of Louise Zabriskie's **Mother and Baby Care in Pictures**[9] is one of the best examples of books for the pregnant woman and the mother of a newborn child, yet published. The text is characterized by brevity and clearness, every non-essential has been eliminated, and the text is medically correct. The outstanding feature of this book and one which makes it so extremely valuable is the profuseness of illustrations, of which there are 204. These illustrations are not only accompanied by full explanatory legends but correlate the text to an unusual degree.

[6]**Contribucion al Estudio del Embarazo Abdominal.** Por Dr. David Orta Menendez. Faculdad de Medicina de la Universidad de la Habana. Tesis de Instructor, 1939.

[7]**Observaciones Sobre la Clinica del Puerperio.** Por Carlos Alexanderson Ruelas. Universidad Nacional Autonoma de Mexico, Faculdad de Medicina. Editorial Cultura, Mexico, D. F. 1941.

[8]**Semiologia do Ovario, com um Estudo Particular da citologia Vaginal.** Par Dr. Francisco Victor Rodrigues, Professor de Clinica Ginecologica da Faculdade Fluminense de Medicina da Universidade do Brasil, etc. Casa do Livro Limitada, Rio de Janeiro, 1941.

[9]**Mother and Baby Care in Pictures.** By Louise Zabriskie, R.N., Director, Maternity Consultations Service, New York City, etc. Second edition, revised and reset. 208 pages with 204 illustrations. J. B. Lippincott Company, Philadelphia, 1941.

There are few steps in the development and early care of the baby from embryology up to the end of the first year, which are not illustrated. This book may be recommended heartily to all expectant mothers and their husbands.

PHILIP F. WILLIAMS.

Miscellaneous

This book, within its 276 pages, contains an epitome of the survey of human nature from the zoological viewpoint. **About Ourselves**[10] is written by James G. Needham, professor emeritus of entomology and limnology. It is not remarkable for new ideas but for the cameolike presentation of a huge concept. Like a cameo, it is clear-cut, precise, delicate but vigorous. I read it from cover to cover with real enjoyment, pleased by the simplicity of its presentation and the large conception of its execution.

The author has traced our structure and development, and our first steps in learning, back to their sources in the animal world, starting with the automatic actions of lower forms, upward to the volitional control of the large brain of the primate.

Although viewed with the broad vision of the biologist, its pages overflow with human insight, kindness and humor, mellowed by age, but through the critical eyes of the entomologist. The main portions deal with man in his biologic aspects, which covers evolution, including the development of behavior, instinct, and learning. Then Part II deals with society in its biologic aspects, which embraces population, social nurture, and the components of social behavior. These components which include physiologic activities, instinct, folkways and reason, are taken up in detail. War, from its biologic aspects, covered from a similar point of view, and finally religion, are discussed. This book should appeal equally to the late adolescent and to the mature scientist.

R. T. FRANK.

Jason's monograph on **Hernia**[11] begins with an extensive historical outline in which the author attempts to give a complete nosography of this age-old common affliction. It appears that hernias were known and described as far back as existent archeologic documents can testify. With the zeal of a true historian, the author has collected numerous texts, antique and baroque, and frequently quotes and annotates them, sometimes showing a little impatience as to the slowness, cruelty, and fancifulness of the human mind in grappling with problems of bodily disorder. All this makes interesting and entertaining reading.

The main part of the book opens with a chapter devoted to statistics. Then follows a detailed description of the regional anatomy, and a discussion of the etiology of inguinal hernia, with numerous quotations from the writings of many authors. The references are all pertinent and some are fundamental and illustrate well the evolution of modern concepts of hernia pathology. However, here as in other parts of the book, the reader misses an occasional summarizing paragraph.

The treatment of hernia has recently been complicated by the revival of the injection methods. A full historical account of the subject and detailed technical steps are given, although the author himself probably has made use of this therapy in a limited fashion. The only type of hernia which he considers amenable to injection treatment is the indirect inguinal one. A chapter on trusses is likewise comprehensive and contains useful details.

Concerning the operative treatment, numerous procedures in vogue yesterday and today are described in detail and with a desire to make the historiography of hernia

surgery as complete as possible. While it is most stimulating to read such full accounts of operative methods, the arrangement of the material makes quick orientation somewhat difficult. For instance, the full description of the Bassini operation, admittedly the keystone of modern hernia repair, is given much later than that of more complicated procedures and mere modifications. Nevertheless the author's discussion of the Bassini operation is excellent, and nowhere can one find a better and more succinct statement of the inherent difficulties of hernioplasty. The author's recommended technique for inguinal hernia varies according to the type. Emphasis is placed on the repair of the transversalis fascia wherever feasible.

Several excellent pictures of unusual varieties and odd contents of hernia sacs are found in the chapter on femoral hernia. The advantages of the inguinal approach for this type of hernia, on account of the better orientation and the greater accuracy in dealing with compromised intestines, are emphasized. Among a total of 1,000 cases of hernia coming under the observation of the author, femoral hernia was encountered in 17 male and 49 female patients. At the same time, inguinal hernia in female patients was still three times more frequent than the femoral type, while in men the ratio was as high as 20:1.

Special chapters are devoted to umbilical, median line, incisional, diaphragmatic, pelvic, sciatic, obturator, and intra-abdominal hernias with descriptions of operative procedures for these, sometimes rare, findings.

In a concluding chapter on recurrent hernia several practical questions are touched upon. Wound infection after repair of an inguinal hernia is not necessarily followed by recurrence. As a matter of fact, in the author's experience, they have been rather the exception. In infants, children, and young adults hernioplasty is unnecessary or harmful because the suture of a well-functioning internal oblique muscle leads to its degeneration. The technique for extensive direct hernia, as advocated by the author, is depicted in this chapter in one drawing. Simultaneous bilateral operations are considered more conducive to postoperative complications and to reduction of permanent results. The author prefers spinal anesthesia and does not seem to belong to the advocates of the silk suture technique.

The third section of the book is devoted to the so-called "compensable hernia," an issue brought before courts and compensation boards innumerable times. Besides a lucid exposition of the etiologic factors which enter into the making of hernia, a comprehensive survey is given of legal procedures and decisions handed down by courts from Alaska to the Straits of Magellan.

The book contains over 350 illustrations, the majority from the very attractive and instructive sketches made by Alfred Feinberg. Literature references, not always complete, are inserted in the text. No separate bibliography is given in tabulation form or as footnotes. The size of the book will limit the extent of its use, but it does contain practically everything about hernia. Perhaps condensation of historical and other material, with rearrangement and more emphasis on the salient and the pertinent, may greatly enhance its handiness.

G. E. GRUENFELD.

The Doctors Mayo[12] by Clapesattle proved most enjoyable reading and should prove so to all medical men who have any interest in the history of the development of American medicine from 1845 on. It deals with two generations of the Mayo family, starting with William W. Mayo, born in England in 1820, who emigrated to the United States in 1845. For a short time he was a pharmacist in the old notorious Bellevue Hospital in New York. By gradual stages during which he practiced all

[12]**The Doctors Mayo.** By Helen B. Clapesattle. Illustrated. The University of Minnesota Press, Minneapolis, 1941.

sorts of professions, including a fancy tailoring establishment in Lafayette, Indiana, he came to Minnesota in 1854. During these years he supplemented his fragmentary medical knowledge by working under Dr. Deming and likewise attending the proprietary medical school of La Porte, Indiana. In Minnesota his activities included exploration of Lake Superior region, farming, veterinarian practice, justice of the peace and ferryman. By 1861 he had established a real medical practice in the region of Le Sueur which was interrupted by a serious outbreak of the Sioux Indians. The senior Mayo finally moved to Rochester in 1864. William J. Mayo was born in 1861 and Charles Mayo in 1864.

The elder Mayo evidently was a wide-awake, community-minded individual who did not shy from work of any kind and who continued to improve his medical knowledge throughout the years. He was the first man to practice ovariotomy in Minnesota, establishing an increasing reputation as a skillful surgeon. His sons, William and Charles, were early initiated into the mysteries of medicine, received as good an education as was possible locally, and eventually graduated as physicians. They started by helping their father who, as well as the sons, made pilgrimages to various medical centers to improve their knowledge which almost always showed some advance over the current medical understanding throughout the country. The gradual increase of their practice and the requirements of the community encouraged the Sisters of St. Francis to start a modest hospital at Rochester from which the present world-famous Mayo Clinic developed. From this modest beginning a slow but progressive growth can be noted. The book shows convincingly how hard work, attention to detail, widespread acquaintanceship, the interest of the community and especially of its newspapers, the constant enlargement of medical acquaintanceship and friendship, blossomed and came to fruition in the present organization which likewise was not planned but developed by evolution.

The rapid growth of the Mayo Clinic was bound to produce jealousies, antagonism, and active hostility, particularly in the neighboring large cities. This resulted in many accusations of unfair practice, of unethical advertising, etc. All of these phases are discussed freely and on the whole impartially. After the death of the senior doctor, and after the two brothers, William and Charles, had reached full maturity, they gave a liberal endowment for the continuation of the Clinic to the University of Minnesota of which it is now a part.

Reading of this volume will be of great interest to the older physicians because they will encounter so many friends and former teachers within its pages. In addition, it gives a most illuminating picture of the growth of American medicine throughout the country. The younger men will profit much by its perusal and will see by what slow and painful stages modern medicine has been born. How great an appeal the book will have for the laity is hard for the reviewer to judge.

The sole discordant notes appearing in this well-written volume, arise from the apparent hesitation shown in writing this volume. There can be no question but that all three Mayos are well worthy of such a careful biography. It is to be regretted that none of them were willing to write an autobiographic report. If some readers who are not in sympathy with group practice and certain evils which have developed therefrom, feel that the treatment accorded by the author to her subjects is too lenient or favorable, this after all, is the common fault of biographers in general.

<div align="right">R. T. FRANK.</div>

Within the past ten years changes in concepts concerning and advances in specific therapy of communicable diseases have been extensive and in some cases bewildering, and therefore there is value in a book which attempts to present what is both old and new and which also sorts the wheat from the chaff. Not

only does **Clinical Immunology, Biotherapy and Chemotherapy**[13] by Kolmer and Tuft cover the diseases caused by bacteria, viruses, and fungi, but it includes discussion of those immunologic processes which are strange and potentially harmful, namely the allergies.

A little more than one-third of the subject matter is devoted to outlining fundamentals concerning the agents of disease and their action, and the basic knowledge relating to immune reactions and the immune antibodies. In this first part, in concise fashion, an excellent presentation of this field is given, so that little that is pertinent to an understanding of infection and specific therapy is omitted.

The second part takes up separately the specific diseases. All forms and aspects of therapy are presented. Prophylactic and curative measures are considered and in many cases a variety of measures are discussed. The material in these chapters is well organized and in addition summaries of the most important points are given at the end of each chapter.

In view of the effort which has been made to place within these pages the complete knowledge of biotherapy and chemotherapy as applied to specific diseases, this volume serves a valuable purpose for reference and consultation.

MOYER FLEISHER.

The importance and constantly increasing use of blood transfusions should make this book, **The Blood Bank and the Technique and Therapeutics of Transfusions,**[14] by Kilduffe and DeBakey, especially timely.

Following a short discussion of the history of transfusion, the authors present an important chapter on the fundamental physiology upon which blood transfusions depend. The indications and recommendations for the use of this measure in hemorrhage and shock and other conditions are described. Following a short discussion of the military aspects of transfusion and the special types of transfusion, the text is largely devoted to the technique surrounding this method, in all its phases. Four chapters are given to a discussion of the blood bank, the technique essential in its institution, the method of operation, and the physical and biochemical changes which may occur in stored blood.

The subject of plasma transfusion follows the same method of presentation. Of more direct importance to the clinician should be the final chapters of the book which describe the methods and technique of transfusion under various circumstances. The final chapter discusses the most frequent complications of blood transfusions and stresses the potential dangers of this often life-saving procedure.

The book is extensively illustrated and the review of the literature is tremendous, one chapter having 650 references. It would seem that such a book as this would be a necessary working manual for the blood transfusion department of all hospitals and clinics.

PHILIP F. WILLIAMS.

A Primer on the Prevention of Deformity in Childhood[15] has been prepared by Dr. Richard Beverly Raney in collaboration with Dr. Alfred Rives Shands, Jr. It

[13]**Clinical Immunology, Biotherapy and Chemotherapy.** By John A. Kolmer, Professor of Medicine, Temple University School of Medicine, etc., and Louis Tuft, Assistant Professor of Medicine, Temple University School of Medicine, etc. 941 pages, illustrated. W. B. Saunders Company, Philadelphia, 1941.

[14]**The Blood Bank and the Technique and Therapeutics of Transfusions.** By Robert A. Kilduffe, Director, Laboratories, Atlantic City Hospital, etc., and Michael DeBakey, Assistant Professor of Surgery, School of Medicine, Tulane University of Louisiana, etc. 558 pages with 214 illustrations and one color plate. The C. V. Mosby Company, St. Louis, 1942.

[15]**A Primer on the Prevention of Deformity in Childhood.** By Richard Beverly Raney, Associate in Orthopaedic Surgery, Duke University School of Medicine, etc. In collaboration with Alfred Rives Shands, Jr., Medical Director, Alfred I. du Pont Institute of the Nemours Foundation, etc. Illustrated by Jack Wilson. 188 pages with 88 figures. National Society for Crippled Children in the U. S. of America. Elmyra, Ohio, 1941.

is distributed by the National Society for Crippled Children at the nominal price of one dollar.

Since the effectiveness of efforts in the prevention of deformities obviously depends upon their prompt application, this volume was written specifically for those who most likely will be the first to see the afflicted child, namely family physician, welfare worker, and health nurse. In accord with this aim the primer is written in plain, simple language avoiding, as far as possible, technical terms. It gives in detail the characteristics, causes, and methods of prevention and treatment of all the more common congenital and acquired conditions prone to result in permanent deformity.

The obstetrician often is one of the first to see such anomalies, whether congenital or unfortunately acquired incident to birth. He cannot fail to appreciate such a ready reference book to inform him of the best procedures to be applied promptly. The value of this little book is greatly enhanced by 88 instructive text illustrations, 37 of them taken from Shands' well known *Handbook of Orthopaedic Surgery*. (The C. V. Mosby Co., 1940.)

HUGO EHRENFEST.

The two fields in which radiation therapy has been proved to be effective and about which much has been published are cancer and dermatology. **The Roentgen Treatment of Infections**[16] by Kelly and Dowell is a text intended to fill the gap which exists in a third great field in which x-ray therapy is effective.

The introductory part of the text deals with x-ray physics and the fundamentals of radiation therapy. This is presented simply and directly and is supplemented by an adequate bibliography. After a review of the background and general considerations of roentgen therapy in infections, the authors undertake an exhaustive discussion of gas bacillus infection. They present their evidence to prove the efficacy of x-ray therapy in gas gangrene, a method of treatment which if used early will, they claim, cut the mortality rate to about 10 per cent. They conclude that, ''only the exceptional patient dies of gas bacillus infection alone if treated with x-rays according to directions.'' In view of the considerable controversy which exists at the present time in the literature dealing with this subject and the lack of controlled clinical investigations, or proved laboratory experimentation, it would seem that the authors have adopted an extreme point of view, which, at the present time, seems open to question. No harm whatsoever can be produced by x-ray therapy for gas gangrene, provided it is used under experienced supervision, and it is hoped that in the present world conflict, the opportunities for its use will be utilized to the utmost with a view to establishing to the satisfaction of all, the specific value of this modality. Radiologists will question the wisdom of the suggestion that because only low voltage x-ray apparatus is used and small dosages of x-ray applied, therefore, the average physician can undertake this type of therapy. A superficial knowledge of x-ray principles does not qualify one for superficial x-ray therapy.

Because of the authors' unusual interest in the treatment of gas gangrene, peritonitis, and pneumonia with x-ray, a disproportionately large part of the book is devoted to these subjects, more than 80 per cent, with the result that there is a tendency to direct emphasis away from the more common, albeit less dramatic and fatal, inflammatory conditions for which radiation therapy can be of value. To the obstetrician and gynecologist, the chapters dealing with parotitis, peritonitis, and acute abdominal conditions will be of particular interest and value.

The authors have permitted their enthusiasm and keen interest in the subject of gas gangrene and its treatment by x-ray to overemphasize some of the material in the text resulting in too great detail and, at times, repetition. For the average physician and surgeon, the material could have been handled more effectively and directly in a smaller, brief monograph.

H. R. SENTURIA.

In **The Microbe's Challenge**,[17] Dr. Eberson has described for the always interested lay public the life history and biologic characteristics of a number of our most potent enemies. This is a fine story of the development of preventive medicine and portrays fundamental advances and principles of microbiology. The outstanding discoveries of Pasteur, Koch, Jenner, and other great men in preventive medicine are described so clearly and interestingly that the text should be of just as much interest to the medical profession as to the laity, for whom the book is intended. This succinct presentation of the major epidemic diseases and the manner in which present-day medicine is fighting such conditions, reflexly should lead to widespread support of present methods in research to eliminate challenges to national and international public health. The book is commended as accurate and informative reading for the lay public.

PHILIP F. WILLIAMS.

Dr. Kahn presents the second edition of his treatise entitled, **Our Sex Life.**[18] While the book is devoted to the problems of sexual relationships, the author has included problems of fertility and infertility. Proceeding to the neuropsychic aspects of sex life, he discusses those situations which are often functional or neurologic in origin. He then presents the diseases of sex life, their complications, and social aspects. There is a section on the nature of prostitution in which the social and legal phases are discussed.

The author returns to sex education in discussing the juvenile sex life and explains the duties of both parents and individual and communal sex education programs. The problems which occur with unmarried people are handled without moralizing. The author offers a sane discussion on the difficult problem of extramarital sexual intercourse. This volume concludes with a well-thought-out chapter on solutions of the sex problem. There are a few medical mis-statements in this book regarding the life-cycle of spermatozoa, the fertile period, and the treatment of nausea and vomiting.

There are few problems concerning sex life which one cannot find in this book and for counsellors on such a topic the comprehensive treatment of the subject may be of value.

PHILIP F. WILLIAMS.

[17]**The Microbe's Challenge.** By Frederick Eberson, Ph.D., M.D., Director of Laboratories, Gallinger Hospital, Washington, D. C. 354 pages. The Jaques Cattell Press, Lancaster, Pa., 1941.

[18]**Our Sex Life.** A Guide and Counsellor for Everyone. By Fritz Kahn. Second, revised edition. 459 pages. Illustrated. Alfred A. Knopf, New York, 1942.

Society Transactions

CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF NOVEMBER 21, 1941

The following papers were read:

Wound Disruption and Its Management. Herbert E. Schmitz and Dr. James H. Beaton, Grand Rapids, Michigan (by invitation). (For original article, see page 806.)

The Use of Ergonovine in the Placental Stage of Labor. Dr. M. Edward Davis and Dr. Melbourne W. Boynton (by invitation). (For original article, see page 775.)

MEETING OF DECEMBER 19, 1941

The following symposium on Hysterectomy was presented:

Vaginal Hysterectomy. Dr. Harry Boysen (by invitation).

Subtotal Hysterectomy. Dr. Lester E. Frankenthal, Jr.

Total Hysterectomy. Dr. Eugene A. Edwards.

Summary. Dr. George H. Gardner.

OBSTETRICAL SOCIETY OF PHILADELPHIA

MEETING OF NOVEMBER 6, 1941

The following papers were presented:

Spontaneous, Painless Parturition in a Case of Pregnancy Complicated by Transverse Myelitis. By Dr. J. Stanley Cohen (by invitation). (For original article, see page 873.)

The Management of Dead Abdominal Pregnancy. By Dr. J. P. Quindlen and Dr. R. C. McElroy (by invitation).

Evaluation of the Metranoikter in Dysmenorrhea. By Dr. S. Leon Israel.

Cotton Suture in Gynecology. By Dr. Saul P. Savitz.

Department of Reviews and Abstracts

Selected Abstracts

Labor

Nakadima, T.: Statistical Study of Elderly Primiparas, Jap. J. Obst. & Gynec. 24: 33, 1941.

The author analyzed the records of 109 primiparas over thirty years of age. In this group he noted the difference between late marriage and lapse of a number of years after marriage before pregnancy took place. Toxemias, long duration of labor, premature rupture of the membranes, weak uterine pains and perineal lacerations were more common than usually. Because of these facts, the author favors cesarean section in cases of breech presentation in an elderly primipara.

J. P. GREENHILL.

Hemmingway, Ruth V., and Chung-Teh, Chou: Report of 729 Obstetrical Cases in Chungking, Chinese M. J. 59: 90, 1941.

Pelvic measurements on women from 16 provinces of China, 710 measurements in all, tend to confirm the observation that the average for China is lower than that for some other countries.

The average blood pressure for the group was systolic 120 and diastolic 80.

A table of the first menstrual periods of 434 women shows that on an average it first appears at the age of 15.2 years (Chinese count).

A study of the complications encountered in this group shows 1 per cent for eclampsia and 1 per cent for placenta previa. Rupture of the uterus occurred in 0.2 per cent, and abruptio placentae in 0.4 per cent.

Of 729 deliveries, 82 per cent were spontaneous, 8.6 per cent were forceps deliveries, and 2.4 per cent were podalic extractions. Three per cent had cesarean sections. Craniotomy was required in 1 per cent and version in 3 per cent.

Head measurements, made on a small number, suggest that heads of Chinese babies do not differ in measurement from those reported in the United States, in spite of the difference in the measurements of their mothers' pelves.

C. O. MALAND.

Cantone, Carlo: Premature Delivery in the Department of Obstetrics and Gynecology of Dr. Vercelli, Folia demograph-gynec. 37: 117, 1940.

The author reviews the literature and considers the many angles of the problem of premature labor. He stresses certain differences in the statistics obtained by himself and those offered by other writers. He confirms the importance of regional and constitutional factors in premature labor. He finally suggests that the working classes, especially the farm women, should desist from their arduous duties during

the latter part of pregnancy in order that the incidence of premature labors and the rate of consequent prenatal deaths be lowered.

MARIO A. CASTALLO.

Kirchner, W.: Twilight Sleep With Dilaudid and Pernocton, Zentralbl. f. Gynäk. 64: 1424, 1940.

The author administers 0.002 Gm. of dilaudid intramuscularly when the patient is definitely in labor. At least three hours later 4.5 c.c. of pernocton is slowly administered intravenously. If it is apparent, however, that delivery will be complete within an hour or less, the pernocton is not given. Although some of the infants have an asphyxiated appearance at birth, in the author's series they all cried strongly and none were lost. Amnesia and analgesia for the labor are highly satisfactory.

R. J. WEISSMAN.

Robertson, Kenneth M.: Intravenous Anesthesia in Obstetrics, Brit. M. J. 1: 815, 1941.

The author recommends intravenous barbiturate anesthesia in obstetrics, increasing thereby the patient's comfort, eliminating the unpleasantness and inconvenience of open ether or chloroform, and relieving the assistants to perform duties other than anesthesia. Intravenous evipan was used during the second stage of labor in over fifty cases including low forceps delivery, breech extraction, and manual rotation with forceps extractions of persistent occipitoposterior positions. One gram of evipan in a 10 per cent solution was used in each case, giving a very complete anesthesia, particularly with earlier premedication as chloral and broximide or morphine. One or two patients with no premedication showed some movements of the legs during delivery. The third stage in each case was uneventful. There were no complications in the progress of mother or child. The patient usually recovered consciousness shortly after delivery.

Smaller dosages were used in 7 cases of spontaneous deliveries with cephalic presentation. One of these infants had some delay in respiration.

Evipan was also used with success in perineorraphies.

FRED L. ADAIR AND WM. ROSENBAUM.

Fuchs, H.: A New Obstetrical Phenomenon: Wry Neck, Zentralbl. f. Gynäk. 65: 619, 1941.

The author reviews the literature on 180° rotation of the head during labor. The condition may be diagnosed by finding on vaginal examination the anterior fontanel to be on the same side as the infant's back as felt by abdominal palpation. Radiographs confirm the finding. The author supports his case with a photograph, showing the infant tolerating 180° rotation with no apparent discomfort. This condition is seemingly innocuous for the life of the infant and may be caused by either rotation of the body on the head during labor contractions or by active rotation of the head on the body.

R. J. WEISSMAN.

Perez, M. L., and Rosenwasser, J.: Neurovegetative System and Uterine Dynamics in Labor, Bol. Soc. chilena de obst. y ginec. 5: 95, 1940.

The authors present, with detailed protocols of 60 cases, their conclusions as to the relation of type of uterine contractions to the status of the patient's vegetative nervous system. Physiologic uterine contractions are in direct relation with good sympathetic excitability. Uterine hypodynamia is found in cases having vagal or

sympathetic hypotonus. In vagotonic individuals the contractions are of a spasmodic irregular nature. The authors feel that prior determination of an abnormal neuro-vegetative status permits a rational therapy at term to bring it into a balance favorable for good uterine contractions.

R. J. WEISSMAN.

Schultze, G. K. F.: The Functional Independence of Each Half of the Uterus, Zentralbl. f. Gynäk. **65:** 2, 1941.

The author presents the evidence of serial radiography of the uterine cavity as outlined by contrast medium to show that each lateral half of the uterus contracts independently of the other. This might have been expected from the duplex embryologic development of the uterus. Its clinical significance is yet to be established, but Schultze feels that it attains importance in a possible explanation of some cases of abortion in which the effect of unilateral uterine contraction may be dislodgment of the implanted ovum. He would like to add this independent contractility as a possible cause of dystocia and thinks it should be considered in prolonged ineffective labor pains where other causes of dystocia cannot be found.

R. J. WEISSMAN.

Lüttge, W.: Full Baths at Term, Zentralbl. f. Gynäk. **65:** 844, 1941.

The author reviews the opinions to be found in the literature on the dangers of a full tub bath at term, especially with regard to the danger of ascending infection after rupture of membranes, to all of which he takes exception. Lüttge favors the full bath with green soap and a chlorine antiseptic added to the water. Where only 5 to 10 liters of water are consumed in a sponge or shower bath, the tub bath affords a great dilution of bacteria with 200 to 300 liters of water. A decrease in puerperal morbidity was ascertained in patients having a forceps delivery after full bath, and the author considers the bath the best predelivery antiseptic. This conclusion is based on results with 12,000 patients with intact membranes and 3,000 patients with ruptured membranes. The psychic influence of the bath is favorable. The bath often stimulates or initiates labor pains. Premature rupture of membranes may be diagnosed by prompt onset of labor with the bath, quinine, and hot applications, and the diagnosis of postmaturity may be excluded if labor starts. Primiparous labor is shortened to ten hours in many cases and to six hours for multiparas.

R. J. WEISSMAN.

Doneddu, F. P.: The Determinative Cause of Labor, Ginecologia 16 (Series 2): 483, 1940.

The author reviews the multiple theories regarding the determinative cause of labor. He covers theories and hypotheses advanced from the Hippocratic epoch to the era of endocrinology. He adds nothing original and is in agreement with prevailing views on endocrine factors.

The material is well arranged. It is presented in a concise and chronologic manner. The article may be of particular value to those who seek continental sources for historical data upon this subject.

CLAIR E. FOLSOME.

O'Sullivan, J. V.: Severe Uterine Inertia Treated by Cutting the Cervix, Brit. M. J. 2: 852, 1939.

A method of expediting cases of severe uterine inertia is described. This consists of cutting the cervix at 3 and 9 o'clock of the clock dial, the incisions extending in-

ward not more than half an inch from the edge of the cervix. The author advises that the procedure be preceded and followed by a hot antiseptic douche. After being cut, the cervix is ''pushed gently up over the front of the head.''

Fourteen cases are discussed, with good results in all cases with the exception of one in which the mother developed septicemia and peritonitis and died twelve days after delivery.

F. L. ADAIR AND E. CHEYDLEUR.

Louros, N., and Kyriakis, L.: Artificial Initiation of Labor—Use of Stilbestrol and Progynon, Zentralbl. f. Gynäk. 64: 957, 1940.

Although in a series of 2,000 cases, weak labor pains as a rule were successfully treated by the use of quinine, heat, and thymophysin, some were found to be absolutely unaffected. It is the opinion of the authors that the initiating mechanism of labor for the most part consists of a sudden flooding of the organism with follicular hormone, sensitizing the myometrium to the influence of posterior pituitary hormone.

Using Cyren (the dipropionic acid ester of dioxydiethylstilbene) Louros and Kyriakis gave 2.5 mg. (equivalent to 5 mg. estradiol) intramuscularly in hourly doses to a total of 10 to 12 mg. in 38 cases in an effort to initiate labor. There was no result in 32 cases, but light uterine contractions in 6 cases. Combining the same dosage of cyren with 200,000 I.U. of progynon, only a few cases showed uterine contractions. In 32 patients who had reached or passed term, the authors followed the above treatment with quinine and thymophysin. Labor began in an astonishingly short time, and 24 primiparas reached the second stage in an average of twelve hours, 8 multiparas in seven and one-half hours, and 9 elderly primiparas in fourteen and one-half hours. No untoward effect was noted on mother or child, and there was no inhibition of lactation.

R. J. WEISSMAN.

Effkemann, G.: Oxytocic Effect of Follicle Hormone, Zentralbl. f. Gynäk. 65: 338, 1941.

The author administered 10 mg. of estradiol by vein to a group of 27 patients at term. Labor began in all patients within eighteen hours, proceeding to delivery. The mechanism of the estradiol effect is discussed, and Effkemann concludes that when administered by vein the hormone exerts not a sensitizing, but an acute and direct effect on the myometrium.

R. J. WEISSMAN.

Friedrich, H.: Clinical Study of Follicle Hormone Initiation of Labor, Zentralbl. f. Gynäk. 65: 613, 1941.

Excluding cases of primary or secondary atony of the uterus, the author administered to a group of women radiographically proved to be past term without labor, large doses of progynon in combination with a small dose of castor oil. If labor was not induced, quinine-thymophysin induction was attempted some hours later. A similar group having the above medication without follicle hormone went into labor on an average three hours sooner. Results in the case of premature rupture of membranes in otherwise normal patients without labor were more promising, as administration of follicle hormone appeared to bring on active labor in a series of 87 cases in an average of 3.7 hours. Contrary to expectation there was no noticeable inhibiting effect on subsequent lactation.

R. J. WEISSMAN.

Gross, Rudolf: **The Occurrence, Significance and Treatment of Premature Rupture of the Membranes,** Ztschr. f. Geburtsh. u. Gynäk. **121:** 163, 1940.

One thousand consecutive obstetric cases were used to study cases of premature rupture of the membranes. By arbitrary definition, premature rupture of the membranes includes all cases in which rupture occurred before the cervix had become half dilated. On this basis, 31 per cent of labors were associated with premature rupture of the membranes, with primiparas showing a little more and multiparas somewhat less than the average incidence. No very significant relationship could be demonstrated between this condition and pelvic contraction, anomalies of position or presentation or size of the child. Multiple pregnancy showed an increased incidence. When premature rupture occurred, labor was shortened but no deleterious effect on mother or child was demonstrable. No therapy is, then, indicated.

J. L. McKELVEY.

Metz, Alfons: **The Effect of Premature Rupture of the Membranes on Duration of Labor,** Ztschr. f. Geburtsh. u. Gynäk. **121:** 199, 1940.

The same thousand cases described by Gross were analyzed further. When rupture of the membranes occurred (spontaneously, presumably) before labor, the latent period averaged eleven to twelve hours with an average first stage of nine hours for the primipara and five hours for the multipara. First stage was thus shorter than average. No effect on the second stage was demonstrated. It seemed that the longer the latent period, the shorter the first stage and vice versa.

J. L. McKELVEY.

Short, C. R.: **Induction of Labor by High Puncture of the Membranes,** Bristol Med.-Chir. J. **57:** 121, 1940.

The author induced labor by high puncture of membranes and withdrawal of 16 to 20 ounces of fluid in 87 cases, 47 of which were primiparas. Toxemia, eclampsia, dystocia, toxemia with twins, hemorrhage, postmaturity, pyelitis, mitral stenosis, insanity, and epilepsy were the indications in this group. Labor was induced from the thirty-sixth week of pregnancy onwards. Due to maternal apprehension a general anesthetic was given for the procedure in 14 cases. Ordinarily hyoscine and morphine are given one hour beforehand. The vagina and cervix are cleaned, and without grasping the cervix, it is gently dilated with one finger and the special cannula-catheter is passed up between the membranes and the uterus to a point above the fetal head where puncture is made. In general, labor began in twenty-four hours. The average duration of labor was fifteen hours for primiparas and eight for multiparas, shorter than in the average normal case at term. The author explains 6 stillbirths in this series as being due to factors other than induction, such as the use of forceps, quinine and pitocin and other unusual measures. The corrected morbidity as measured by pyrexia was 2.3 per cent, although the temperature in the two cases involved did not rise above 100.4° F. Shorter labor and salvage of more mothers and infants are the author's justifications for a wider use of high puncture of the fetal membranes.

R. J. WEISSMAN.

Gairdner, Alan, Hadley, Margaret, and Jackson, L. N.: **A Hundred Cases of Breech Presentation,** Lancet **1:** 273, 1941.

Of 100 consecutive cases of breech presentation in hospital and private practice, 11 were treated successfully by version and delivered as vertices; 26 were delivered by cesarean section, and 63 by the vagina. There was no maternal mortality

but the total of stillbirths and neonatal deaths was 19, only one (a monster) being among the infants delivered by cesarean section. Twenty-seven of 53 breech deliveries in the hospital series were by cesarean section while none of the 36 breech deliveries in the private practice series was by section. Ten of the infant deaths were in the first series and 9 in the second.

The authors state that if version fails, cesarean section is the treatment of choice, especially in primiparas or where some degree of pelvic contraction is diagnosed. Breech vaginal delivery is less risky to the child in multiparas than in primiparas.

<div align="right">CARL P. HUBER.</div>

Brunner, C.: Attempt to Hasten the Placental Stage and Diminish the Loss of Blood, Monatschr. f. Geburtsh. u. Gynäk. 111: 249, 1940.

The author modified the method of Mojon and Gabaston for hastening separation of the placenta. Immediately after ligating the umbilical cord, the injection into the umbilical vein was started if there was evidence of ''uniform adherence of the placenta.'' At first the fluid injected consisted of a sodium chloride solution with calcium, adrenalin, anterior pituitary, and gynergen. Because this did not produce the desired results, the solution was changed to a concentrated sodium chloride solution (20 to 30 per cent) with glucose (30 to 40 per cent) similar to the solution used for obliterating varicose veins. In a series of 500 cases, the results obtained by this procedure are encouraging. Thus, in the group where this method was used, the incidence of atony of the uterus was 3.8 per cent, whereas in the control group it was 11.8 per cent. Likewise, in the injection group, the uterus had to be explored for placental remains in 0.8 per cent, whereas in the control group this was necessary in 3 per cent of the cases. Manual removal of the placenta was resorted to with equal frequency in both groups.

<div align="right">J. P. GREENHILL.</div>

Farquhar, Murray: Causes of Post-Partum Haemorrhage, Brit. M. J. 2: 1180, 1939.

Uterine massage following delivery is probably unnecessary although it is the ''general rule'' in England.

If a patient lies for a long time on her side before the placenta comes away the uterus tends to fall up into the abdomen and a disturbance of the neuromuscular mechanism is produced which causes bleeding.

If several attempts at placental expression result only in the expression of large clots, manual removal should be done while the patient's condition is still good.

Some cases of profuse hemorrhage following the third stage may be due to the presence of unusually large arterial trunks close to the placental site.

The author prefers never to pack a uterus but to use bimanual compression followed by a hot douche.

<div align="right">F. L. ADAIR AND E. CHEYDLEUR.</div>

Hoff, F., and Spannagel, T.: Post-partum Ice-Bag Prophylaxis, Zentralbl. f. Gynäk. 64: 945, 1940.

The authors' method of hastening the third stage of labor and diminishing the usual blood loss is to place a heavy (1,200 Gm.) ice bag over the uterine area immediately after the delivery of the child. Two series of 2,000 cases each, comprising material from the Heidelberg Clinic, were compared in regard to the weight of blood lost post partum, one group receiving the so-called ice-bag prophylaxis.

The crude figures show a hemorrhage of over 1,000 Gm. in 0.55 per cent of ice-bag cases as against 2.6 per cent in cases without this prophylaxis. Similar differences appeared in other groups in which bleeding was less. When the two series were broken down into groups with and without lacerations, spontaneous and operative deliveries, a like result appeared in favor of the use of the ice bag. The duration of the third stage in 0.25 per cent of ice-bag cases was over one hundred and twenty minutes as against 0.65 per cent without ice bags.

Comparing various procedures carried out in the immediate post-partum period, the most common was the Credé expression of the placenta with and without narcosis in 12 cases followed by application of ice bags and 45 in which these were not used. Puerperal complications were found in 373 of the untreated cases and 254 in which cold was applied.

R. J. WEISSMAN.

Hoffstrom, K. A.: A Series of More Than 1,000 Forceps Deliveries, Monatschr. f. Geburtsh. u. Gynäk. **112:** 12, 1941.

The author reports a series of 1,047 forceps deliveries performed during the last thirty years at the Tammesfors Clinic. This is an incidence of 4.6 per cent for forceps deliveries. There were 502 outlet forceps, 329 midforceps, and 219 high forceps operations. The corrected fetal mortality in these groups was 2.1, 4.1, and 8.5 per cent, respectively. The author emphasizes that experience has shown the importance of replacing high forceps operations by cesarean section, particularly in cases where there is cephalopelvic disproportion. He is opposed, however, to the widespread use of cesarean section without thorough examinations.

J. P. GREENHILL.

Dietrich, H. A.: Forceps on Aftercoming Head, Zentralbl. f. Gynäk. **65:** 526, 1941.

The author reviewed 17,070 deliveries from 1927 to 1937. The incidence of primary breech presentation was 4.7 per cent. An additional 111 cases were converted to breech for extraction. Twenty cases were sectioned and 906 were delivered with the aftercoming head, of which 40 per cent delivered spontaneously, leaving 556 who required manual or forceps assistance. Of 325 infants delivered with manual assistance, 18 per cent were either stillborn or died in their first ten days. Of 231 having forceps applied to the head, 9 per cent were stillborn or died in the first ten days. Dietrich emphasizes the increased safety for the child with the application of the forceps and discusses in detail the application in various positions of the head.

R. J. WEISSMAN.

Bock, A.: Separation of Symphysis in Spontaneous Delivery, Zentralbl. f. Gynäk. **65:** 494, 1941.

Bock reviews the statistics on symphysial separation and notes in the study of latest world literature an increase in the percentage of separations in spontaneous delivery from 17 to 65 per cent. This is a relative increase and is due in large part to the decrease in high forceps operations as well as a general decrease in the proportion of operative deliveries from below as result of the improvement in radiographic diagnosis and cesarean section. Radiography is important in this condition more to differentiate between loosening and rupture of the joint than merely to make a diagnosis of symphysial traumatization since the symptoms of rupture are characteristic, but there are cases in which roentgenologically there is definite separation

without clinical symptoms. Two cases of separation in primiparas are cited by Bock. In one case symptoms appeared immediately after delivery, and in the other after twenty-four hours. Both were cured by application of a broad pelvic swathe. The author has no explanation for these accidents. The first patient was of a gracile type, but her baby weighed only 3,500 Gm.; the second had a 4,250 Gm. infant but her pelvis was entirely adequate. The author feels all such cases should be reported, if only for their medicolegal significance. The physician involved in litigation, when this accident has occurred in association with forceps delivery, is justified in asserting that symphysial separation can and does occur with spontaneous birth.

R. J. WEISSMAN.

Häutsch, L.: Symptomless Course of Uterine Rupture Due to Incarceration of Placenta in Cesarean Scar, Zentralbl. f. Gynäk. **64:** 1818, 1940.

A 29-year-old gravida v had a cesarean section delivery of her fourth child 3 years previously. A week before hospitalization she experienced severe abdominal pains while doing her housework. Her physician noticed nothing abnormal on examination, except a yellowish vaginal discharge, and as the pain subsided the patient continued her work. Two days before hospitalization severe pain again recurred and continued. After a prolonged labor, a dead infant was delivered, and the patient seemed in good condition except for slight motor restlessness and heavy breathing. The placenta, however, was not forthcoming, and fifteen minutes later the patient went into collapse and died within half an hour. At autopsy almost 2 liters of free blood were found in the abdomen. A large clot filled the left iliac fossa. The genital tract was removed in toto and at the site of the old uterine scar, where the wall had thinned to almost 1 mm., there was a perforation several centimeters in diameter, through which protruded placental tissue. The placenta had been implanted over the site of the scar. The author concludes that the rupture took place two days before admission, when the patient for the second time had experienced pain and dizziness. The placenta had apparently successfully plugged the tear until actual labor set in.

R. J. WEISSMAN.

Gauss, C. J.: A New Craniotomy Instrument: The Würzburg Basiothryptor, Zentralbl. f. Gynäk. **65:** 624, 1941.

The author describes in detail a new basiotribe whose essential new feature seems to be in the fenestrated outer blades which are open like those of a Piper forceps. The distal curve, however, is almost flattened, giving the advantages of a larger grasp on the fetal head without the possibility of engaging tissues on the infant's lower neck and shoulders.

R. J. WEISSMAN.

Dr. Joseph Bolivar DeLee died at his home in Chicago, April 2, 1942. An extended obituary will appear in the June issue of the JOURNAL.

Joseph Bolivar DeLee
1869—1942